

Phenytoin induced Stevens-Johnson syndrome: a case report**Shambhavi Kulkarni*, A. N. Dattatri**

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ABSTRACT

Toxic epidermal necrolysis (TEN) and Stevens-Johnson syndrome (SJS) are rare but potentially life threatening cutaneous adverse drug reactions. Drugs commonly implicated are anti-microbials, anti-epileptics and non-steroidal anti-inflammatory drugs (NSAIDs). Amongst anti-epileptics, carbamazepine and phenytoin are the most common offending drugs. We report here a case of SJS due to phenytoin.

Keywords: Phenytoin, SJS, Seizure, TEN**INTRODUCTION**

According to WHO, adverse drug reaction is defined as “any response to drug which is noxious or unintended and occurs at a dose normally used in man for prophylaxis, diagnosis or treatment of diseases or for modification of physiological function”.¹ ADRs may be said to be the inevitable price we pay for the benefits of modern drug therapy. Yearly estimates of the proportion of outpatients with an adverse drug event range from 5% to 35%.² The relative risk of Stevens Johnson syndrome and toxic epidermal necrolysis, perhaps the most important severe cutaneous reactions have been found to be due to sulfonamide antibiotics, amine antiepileptic (phenytoin and carbamazepine), lamotrigine and oxicam NSAIDs.³ We report here a case of Stevens Johnson syndrome due to phenytoin.

CASE REPORT

A 14 year old girl presented with chief complaint of fluid filled skin lesion all over the body. She was admitted to the Department of Dermatology, KIMS, Hubballi. Patient had 3 days history of fluid filled lesions in the mouth and over the lips, which then burst open leaving erosions over both lips and oral cavity. The fluid filled lesions then developed on neck, back, trunk, both hands and legs which increased in size over few hours. Patient had 2 days history of fever for which she consumed one dose each of tablet paracetamol 500mg and tablet cefixime 200mg. Past medical history is remarkable for epilepsy. She had her first episode of seizure one year back for which she did not receive any treatment. This was diagnosed one month back when she had another episode of seizure, for which she was prescribed tablet phenytoin 100 mg once daily. The

patient was on treatment with the same since then. She had no known drug allergy and had no significant family history. There was no history of joint pain or abdominal pain. Patient however, complained of decreased appetite and disturbed sleep for 3 days. Physical examination: Patient was moderately built, febrile and was well oriented. On dermatological examination, multiple vesicles over the trunk, back, face and both upper limbs and lower limbs were noted. Multiple bullae on trunk and back were seen. She had eroded lesions and white slough on the lips and in oral cavity. Lesions were also seen on the genitalia. On ophthalmic examination, blepharitis was present.



Figure 1: Erosions on the lips.



Figure 2: Multiple vesicles over the abdomen.

Laboratory investigations included a total leucocyte count of 7200cells/cumm, serum creatinine- 0.7mg/dl, blood urea- 29mg/dl, AST- 32IU/L, ALT- 31IU/L, alkaline phosphatase- 61IU/L, total protein- 5.7g/dl, HIV I/II antibodies alkaline phosphatase and HBsAg were negative.

Diagnosis and management

The patient was diagnosed to have Stevens Johnson Syndrome induced by phenytoin with a SCORETEN score

of 3. Phenytoin was immediately stopped and was replaced with tablet levetiracetam. She was treated with dexamethasone, co-amoxiclav, cyclosporine and moxifloxacin eye drops. She was also given meropenem gel and metronidazole for topical application, chlorhexidine mouth wash and paracetamol.



Figure 3: Bullae on the palms.



Figure 4: Bullae on the neck.

DISCUSSION

Toxic epidermal necrolysis (TEN) and Stevens Johnson Syndrome (SJS) are severe adverse cutaneous drug reactions that predominantly involve the skin and mucous membranes. They are characterized by mucocutaneous tenderness and typically hemorrhagic erosions, erythema and more or less severe epidermal detachment presenting as blisters and areas of denuded skin. Currently, TEN and SJS are considered to be two ends of a spectrum of severe epidermolytic adverse cutaneous drug reactions, differing only by their extent of skin detachment. In SJS less than 10% of body surface area is involved and in TEN more than 30% is involved.⁴ Drugs are identified as the main cause of SJS/TEN in most cases, but Mycoplasma pneumoniae and Herpes simplex virus infections are well documented causes.

Several drugs are at 'high' risk of inducing TEN/SJS including: Allopurinol, Trimethoprim-sulfamethoxazole and other sulfonamide antibiotics, aminopenicillins, cephalosporins, quinolones, carbamazepine, phenytoin, phenobarbital and NSAIDs of the oxamic type. Amongst anti-epileptics, phenytoin and carbamazepine have been reported to be the most common cause.⁵ Genetic susceptibility to SJS and TEN is likely. Risk of developing SJS/TEN in patients who carry HLA-B*1502 allele is very high.⁶ Diagnosis relies mainly on clinical signs together with the histological analysis of a skin biopsy showing typical full thickness epidermal necrolysis due to extensive keratinocyte apoptosis. Differential diagnosis includes linear IgA dermatosis and paraneoplastic pemphigus, pemphigus vulgaris and bullous pemphigoid, acute generalized exanthematous pustulosis (AGEP), disseminated fixed bullous drug eruption and staphylococcal scalded skin syndrome (SSSS). Hence it is essential to take detailed drug history of the patient.

Typical clinical signs initially include areas of erythematous and livid macules on the skin, on which a positive Nikolsky sign can be elicited. Mucosal, including ocular, involvement develops shortly before or simultaneously with skin signs in almost all cases. The prognosis of a case of SJS/TEN is made using a validated SCORTEN disease severity scoring system. Patients with a SCORTEN score of 3 or above should be managed in an intensive care unit. The earlier the causative drug is withdrawn, the better the prognosis, and that patients exposed to causative drugs with long half lives have an increased risk of dying.⁷

Various authors have reported varying incidences of SJS with phenytoin. In a study, 28.8% of all SJS/TEN cases were due to antiepileptic agents of which, phenytoin was the most common drug.⁸ She was prescribed phenytoin, following consumption of which the patient developed SJS.⁹ Bhanu et al reported a case of SJS in a 30 year old female who had received phenytoin for seizure disorder.¹⁰ Causality analysis using Naranjo's scale showed that phenytoin is the probable cause of the adverse reaction in our case (score=6).

SJS/TEN is a life threatening condition and therefore supportive care is an essential part of the therapeutic approach. It involves management of fluid and electrolyte requirements. Prophylactic antibiotic use is recommended. Use of corticosteroid in management of SJS is controversial. If steroids are to be used it should be initiated during initial stage (within 72 hours) and rapidly tapered off.¹¹ Early administration of high-dose immunoglobulin has been recommended.¹² The mortality rate of SJS and TEN is high. Renal involvement can occur in such cases causing proteinuria, haematuria, azotemia. Bacteremia/sepsis is usually the cause of death in these cases. In the present case however, patient recovered well with the given treatment.

CONCLUSION

From this study it was concluded, knowledge of the past medical history of the patient regarding past drug allergy, family history of drug allergy or death in the family due to a drug is of great importance in order to avoid morbidity and mortality associated with SJS and TEN. It is of utmost importance to be vigilant while administering drugs known to cause SJS. Early diagnosis, identification of the culprit drug, its prompt withdrawal and specialized supportive care is the key to management of a case of SJS. Since phenytoin is one of the commonest antiepileptic drugs to cause SJS and TEN, its use for seizure prophylaxis and treatment needs to be reconsidered in view of safer alternatives available.

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