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Case Report

Phenytoin-induced Stevens-Johnson Syndrome: A case report

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Abstract Stevens-Johnson syndrome (SJS) is a rare but serious and often life-threatening acute mucocutaneous reaction. Majority of cases are drug-induced resulting extensive exfoliation which may cause severe dehydration and mortality. An-18 year old female reported with chief complaint of generalized edematous erythematous rash with multiple hyperpigmentation on the skin of the face, neck, chest, back, bilateral extremities, and genital area. These acute skin reactions were evoked after consumption of phenytoin and she was treated with corticosteroids, antibiotics, and other symptomatic treatment. Clinicians must be adept at identifying hypersensitivity reactions especially SJS which is a potentially fatal condition. The most commonly prescribed drug regimens which may induce drug allergy should be used judiciously, and alternative safer regimens may be considered if available.

Key words
Drug reaction; Stevens-Johnson syndrome; Phenytoin; Acute mucocutaneous reaction; Anticonvulsant.

Introduction

Stevens–Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN) are life-threatening acute mucocutaneous reactions. Each causes widespread necrosis and epidermal loss typically involving the mucous membrane, separating the dermal-epidermal junction. The resulting generalized exfoliation may cause dehydration and increase predisposition towards infection, which can lead to multiorgan damage or failure.[1,2]

Drug allergy is the known primary cause of SJS and TEN, although infection and malignancy are also potential triggers. Drugs best known to induce SJS and TEN include antibiotics, non-steroid anti-inflammatory drugs (oxycam derivates), antipyretics, and oxide inhibitors.[1,3,4] Herein, we report a female patient who develop acute drug reactions caused by phenytoin. We discuss the diagnosis and management of this condition.

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Case report

An 18-year old female presented to the emergency department with a chief complaint of generalized edematous erythematous rash, accompanied by sore throat, generalized itch, and burning sensation. Skin lesion manifested one day after onset of fever. Based on history taking, she had no history of allergy. Upon physical examination the patient was compos mentis. She was tachycardic, but otherwise her

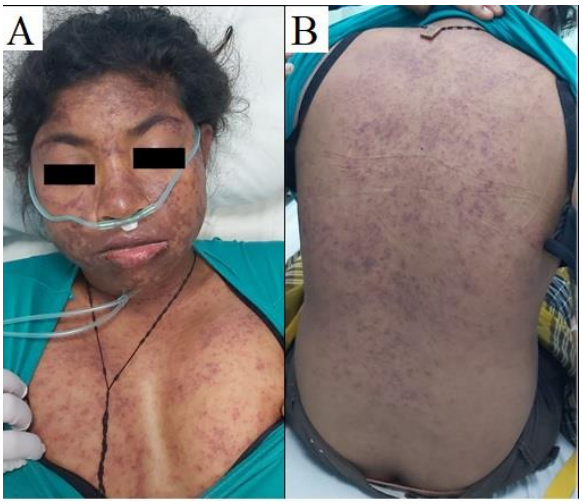

Figure 1 Erythematous macules distributed throughout the face, neck, chest (A) and back (B).

vital signs were within normal limits. The orbital area appeared edematous. Yellowish eye discharge, cilliary injections, and conjunctival injections were found. The lips were edematous and the commissures were eroded, accompanied by dark crusts. Erythematous macules with multiple hyperpigmentation were discovered on the face, neck, chest, back, bilateral extremities, and genital area **(Figure 1-3)**.

The patient is epileptic since 6 months old. The latest epileptic episodes were tonic-clonic seizures occurring three times within the last month. The patient was prescribed phenytoin by a neurologist, taken twice a day, to control her symptoms. The chief complaint manifested two weeks after drug initiation. Blood test revealed leukocytosis with neutrophilia, elevated LED, and mild hypokalemia. ECG and chest x-ray were within normal limits.

The patient was diagnosed with phenytoin-induced SJS and the drug was promptly stopped. Diazepam was chosen as the alternative drug should seizures occur. She received immediate fluid resuscitation with ringer lactate, hypokalemia correction with 25 mEq KCl drip given in 8 hours followed by maintenance with aminofluid and normal saline. Twice a day

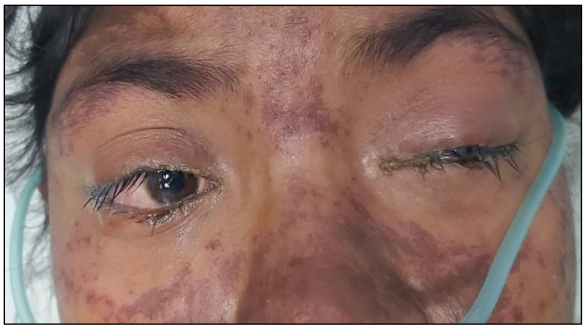

Figure 2 Bilateral palpebral edema with yellowish eye discharge.

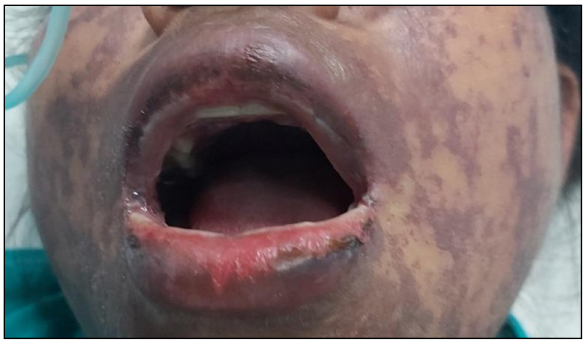

Figure 3 Oral ulcers accompanied by dark crusts.

125mg methylprednisolone injection was delivered for 3 days, then it was then down titrated to 125 mg once a day, 62.5 mg twice a day, and 62.5 mg once a day. Eventually the injections were switched to oral therapy with 16mg methylprednisolone, twice a day. Ceftriaxone injections were given as a prophylaxis against infection. Skin and vaginal lesions were compressed with normal saline, thrice a day, followed by administration of fucidic acid salve. Tobramycin and dexamethasone eye drops were prescribed for the eyes. After two days of hospitalization, edema around the palpebra and lips improved, and no new skin lesions developed.

Discussion

Occurrence of SJS/ TEN may commence anytime from four days until up to four weeks after culprit drug initiation. Nonspecific prodromal symptoms such as malaise, rhinitis, sore throat, fever, pruritus, and eye irritation

may be found two to three days before skin lesions start to manifest.[5] In our case, an 18-year-old female patient experienced a hypersensitivity reaction after two weeks of phenytoin administration. Prodromal symptoms preceded her facial edema as well as skin and mucosal lesions. Under 10% body surface area (BSA) was affected; thus the patient was diagnosed with SJS.

Prevalence of drug-induced SJS and TEN are increasing, with mortality nearing 40%.[6] Among anticonvulsants, phenytoin and carbamazepin are the most common culprits. Banu *et al.* reported a similar phenytoin-induced SJS in a woman.[7] Lobao B *et al.* elaborated a case of TEN in a patient with meningioma who received phenytoin as a prophylaxis against epilepsy.[8] Another TEN case in a patient with epilepsy was also found by Schmidt D *et al*.[9]

There are numerous undergoing studies which look into the molecular pathogenesis of SJS and TEN - results often contradict and no definite conclusion has been able to be drawn. Several studies reported the involvement of a genetic factor, the human leucocyte antigen (HLA) genotype, in the role of drug metabolism in drug hypersensitivity or other immune reactions. HLA-B*1502 is often associated with phenytoin-induced SJS.[6,11-13] As SJS and TEN show rapid clinical deterioration and may lead to unstable condition, clinicians must be aware of this skin manifestations and evaluate more about causes and precipitating factors of the condition. In our case, phenytoin was considered as the culprit of this drug allergic reaction. Therefore, in the future, before prescribing the drug, the history of previous drug allergies, family history of drug allergies or family death due to specific drugs must be fully known.

Early diagnosis and immediate cessation of the suspected cause are the essential first steps in SJS/TEN management, which also includes administration of systemic corticosteroids, fluid therapy, symptomatic therapy, and wound care. During observation, our patient showed satisfactory result and improved skin condition, and she was discharged after one week of hospitalization. A follow-up was conducted one week after. The patient demonstrated generalized skin hyperpigmentation with xerosis without new skin lesions.

Conclusion

Awareness of potential SJS or TEN-inducing medications, early diagnosis, prompt cessation of the culprit drug, and adequate therapy are essential to limit morbidity and mortality. Nutritional and fluid balance is maintained through a holistic approach to improve recovery time. It is crucial that doctors are adept at identifying hypersensitivity reactions such as erythematous rash, vesicobullous lesion, and prodromal symptoms–fever, nausea, sore throat, and abdominal pain. As phenytoin has been named a culprit drug on several other cases, the use of phenytoin as a seizure prophylaxis might have to be reconsidered, if other safer alternative therapies are available.

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