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Case Report

Phenytoin induced Lyell's syndrome: a case report

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ABSTRACT

Lyell's syndrome commonly known as Stevens–Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) is a type of severe allergic reactions affecting the skin and mucous membranes. If surface area of the body (BSA) involvement is less than 10% which is called as SJS and TEN is defined as epidermal detachment >30% of the total body surface area while both SJS and TEN can have involvement of mucosa. BSA with 10–30%, there is overlapping of SJS and TEN. We report a rare, life-threatening case of Lyell's syndrome who presented lesions involving 30% of BSA after the oral intake of phenytoin and she was successfully treated with high-dose steroids and supportive care.

Keywords: Lyell's syndrome, SJS, TEN

INTRODUCTION

Epilepsy (seizure disorder) is a common neurological disorder that affects people globally. It is relatively common condition characterized by a tendency for recurrent seizures, which is due to the disturbance of spread of electrical discharge of the cortical neurons.[1] Phenytoin (5,5-diphenylhydantoin) is one of the most effective and widely prescribed drug for the treatment of epilepsy, which was found to cause toxic epidermal necrolysis (TEN) or Stevens–Johnson syndrome (SJS) more frequently.[2] Despite the inherited risk of dose related toxicity attributed to its zero-order pharmacokinetics, Phenytoin is still considered a first line drug therapy for some types of seizure disorder.[3] Adverse drug reactions (ADRs) are one of the most leading causes of death among hospitalized patients and occur in between 0.3 to 7 per cent of all hospital admissions.[4] These may vary from mild rashes to severe reactions such as SJS and TEN. Mostly anti-epileptic drugs (AED) are associated with increased risk of adverse reactions.[4] Nearly 10% to 15% of patients receiving AEDs, cutaneous reactions, such as maculopapular or erythematous pruritic rash, may appear within 10th to 14th day AEDs administration.[3] Lyell's syndrome is commonly known as drug induced reaction rather than a skin disease.[5]

CASE REPORT

A 48-year-old woman who had presented with generalized tonic clonic seizures (GCTS), was started with oral phenytoin 100 mg twice a day. After 8 weeks of therapy, she developed widespread, pruritic, erythematous, papular lesions all over her body and her skin become scaly and black.

Her vitals were stable. Physical examination revealed bullae were noted over her arms, forearms, legs and buttocks with areas of intense inflammation especially over her eyes, lips and nose. Oral mucosal ulcerations were present. Nikolsky sign was found to be positive. Genital mucosa was normal.

Extensive erythematous plaques were present over the rest of the body (more than 30% of the body surface). Clinical diagnosis of toxic epidermal necrolysis due to phenytoin was made and immediately the offending drug was stopped.

Investigations revealed elevated total leucocyte count with neutrophil predominance, C-reactive protein (CRP) was high and she had hyponatremia along with hyperkalemia.

Procalcitonin was elevated. Various parameters were monitored, paying special attention to urine output and balancing fluid and electrolyte disturbances.

Treatment consisted of fluid infusion, systemic steroids (methyl prednisolone), prophylactic broad-spectrum antibiotics (meropenem) and pain management were done. Infection control measures with sterile hand- ling and reverse-isolation procedures, daily dressings and repeated cultures of the skin, as well as blood and urine, were performed. Ocular and conjunctiva were managed with extensive lubrication of the eyes and local antibiotics, and management of synechiae between the eyelids and conjunctiva. Oral ulcers were treated by applying local sucralfate. She improved and was discharged with low dose oral prednisolone.

Figure 1: The extensive skin and oral lesions on (a) day 1 and its recovery on (b) day 5 and (c) day 9.

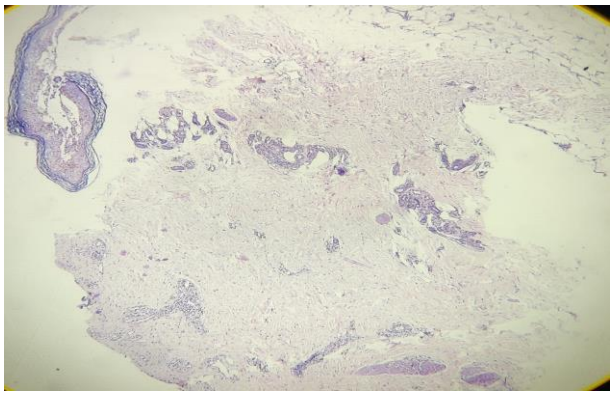

Figure 2: Histopathology section showing subepidermal bulla.

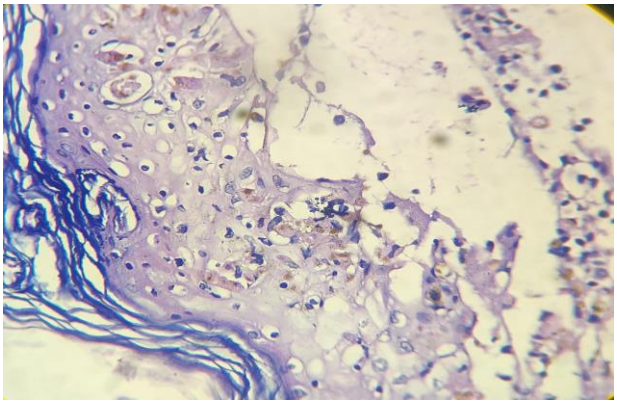

Figure 3: H&E: section shows apoptotic keratinocytes in the separated epidermis.

Skin biopsy was done which showed skin with basket weave keratin and subepidermal bulla (Figures 2 and 3). The epidermis shows scattered numerous apoptotic keratinocytes and few lymphocytes. The upper and mid dermis shows mild perivascular lymphocytic infiltrate. These features were suggestive of toxic epidermal necrolysis.

DISCUSSION

Phenytoin has a narrow therapeutic index of 10-20 mcg/ml.[2] At plasma concentrations below 10 mcg/ml, elimination follows first order. However, at higher concentrations, including those in the therapeutic range (10-20 mcg/ml), the metabolic pathway becomes saturated and elimination shifts to zero order. Half-life of phenytoin varies between six and twenty-four hours at plasma concentrations less than 10 mcg/ml, but increases with higher concentrations. As a result, the plasma concentration rises disproportionally even with small increases in the dose. Toxicity generally correlates with the increasing plasma levels. The increased half-life due to zero order pharmacokinetics can also result in prolonged duration of toxic symptoms.[2]

Currently TEN is considered as a clinically distinct disorder, earlier SJS was considered to be part of a spectrum of erythema multiform (EM) and is part of the SJS-toxic epidermal necrolysis (SJS-TEN) spectrum, characterized by heterogeneous cutaneous bullous eruptions which can result in sloughing of the epidermis. BSA with 10-30%, there is overlapping of SJS and TEN.[6,7]

SJS-TEN overlap falls in between SJS and TEN. Patient may initially present with SJS, which subsequently evolves into TEN or SJS TEN overlap.[4] In this case the patient was presented with red colored skin lesion associated with pain, over face and trunk which is insidious in onset. This gradually progressed to involve the extremities and genitalia. The lesion then became fluid filled and ruptured spontaneously to leave behind raw areas. Likewise, there are reports of phenytoin induced hypersensitivity reactions, erythematous lesions.[4,8] As

soon as the diagnosis of phenytoin induced TEN was confirmed, patient was discontinued for the same and was replaced with levetiracetam 500 mg twice a day as an alternative to phenytoin. Levetiracetam is increasingly being used as an alternative when there comes a need for phenytoin replacement.[4] Hence in the current case the replacement of phenytoin with levetiracetam was a right decision for better patient care and reduce further consequences of phenytoin toxicity.

CONCLUSION

Toxic epidermal necrolysis is a rare severe life-threatening complication associated with use of AEDs like phenytoin which may have familial tendency. Proper counselling to the patient regarding the use of medications is of at most importance, in such life-threatening conditions where treatment guidelines remain hazy. It is also advisable to give personal “drug allergy card”- in the true sense being an alert card about the description of adverse drug reaction to the patient who suffered from such serious reactions.

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