

Toxic Epidermal Necrolysis induced by Phenytoin: A Case Study

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ABSTRACT

Toxic epidermal necrolysis (TEN) is severe adverse cutaneous drug reaction that predominantly involves the skin and mucous membranes. It is usually induced by medications. Anti-convulsants such as phenytoin, carbamazepine and phenobarbital have been enlisted as high risk drugs for causing TEN. **Objectives:** The main objective of this case report is to evaluate the importance of detection, assessment and reporting of an adverse drug reaction and to improve the medication adherence. **Methods:** This is an observational type of case report which we observed in our hospital on regular ward rounds. **Results:** This is a case report of Toxic epidermal necrolysis due to a Phenytoin which was used in the treatment of epilepsy in a 25 year old female patient. Causality assessment of the event with Naranjo' scale suggest "Probable". **Conclusion:** Proper counselling to the patient regarding the use of medications is of utmost importance, in such life threatening conditions where treatment guidelines remain hazy.

Keywords: Adverse drug reaction, Toxic epidermal necrolysis, Phenytoin

INTRODUCTION

Toxic epidermal necrolysis also known as Lyell's syndrome is a rare but potentially life threatening condition.¹ It is rare and affecting approximately 1 or 2/1, 00,000 annually, and it is considered medical emergency as it is potentially fatal.² It is characterized by mucocutaneous tenderness and typically hemorrhagic erosions, erythema and more or less severe epidermal detachment presenting as blisters and areas of denuded skin. Cases with epidermal detachment in less than 10% of body surface area (BSA) are designated as Steven Johnson syndrome (SJS); those with more than 30% of BSA are labelled as toxic epidermal necrolysis (TEN); while cases between 10 and 30% of involvement are defined as SJS-TEN overlap.³ The affected skin may develop flaccid bullae and may detach irregularly, sometimes in large sheets with just a sliding touch (Nikolsky's sign). The consequences of such a massive loss of epidermis include dehydration, increased energy expenditure

and local or systemic infection such as septicemia.⁴ Drugs are identified as the main cause of TEN in most cases. Several drugs are at "high" risk of inducing TEN; the drugs with the highest estimated incidence include co-trimoxazole (trimethoprim-sulfamethoxazole), sulfadoxine-pyrimethamine, and carbamazepine, phenytoin, phenobarbital and NSAIDs of the oxicam-type.^{2,5} TEN is severe and life threatening. We are reporting such an interesting case of phenytoin induced toxic epidermal necrolysis, details of this case is mentioned below.

CASE DESCRIPTION

The patient was a 25 year old woman who had been diagnosed 2 months earlier with convulsions. Treatment was started at that time with phenytoin 100 mg twice a day which was prescribed for duration of one and half month. After receiving drug phenytoin for 46 days of 91 doses she develops widespread, pruritic, erythematous, papular lesions, and skin becomes scaly and black

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all over the body. Excess peel out of skin with intense inflammation of eyes, lips, nose, vagina and ears leads to blockage. On physical examination, the patient presented a temperature of 38°C and a blood pressure of 110/70 mm Hg. On examination there were ulcerated lesions on the oral mucosa. Extensive erythematous plaques were present over the rest of the body (more than 30% of the body surface). The patient was admitted to hospital with a diagnosis of toxic epidermal necrolysis due to phenytoin. Causality assessment of the event with Naranjo' scale suggest "Probable".

As stated above we can see the kind of effects which phenytoin has induced on this patient in the following figures in which figure number 1 is before the treatment and figure 2 is after the treatment.

DISCUSSION

Toxic epidermal necrolysis also known as Lyell's syndrome was first described by Lyell in 1956. The word toxic alludes to the constitutional symptoms while necrolysis refers to the necrosis and detachment of the full thickness of the epidermis.⁶ TEN and SJS are related mucocutaneous disorders with an estimated incidence of 0.4–1.2 patients per year.^{7,8} Both diseases are associated with high rates of morbidity and mortality. Overall mortality for SJS ranges from 5% to 25%, and that for TEN ranges from 15% to 40%. In TEN, maximal rash

involvementis reached within 4 days, and sometimes within hours, whereas the corresponding time for SJS is 1–14 days. About 90% of patients with TEN develop painful erosions in their mucosal membranes, approximately 85% have conjunctival lesions, and about 35% of those who survive experience ocular sequel.⁸

In the present case, the patient was admitted to the hospital with severe rashes, peeling of skin as scales all over the body. On physical examination patient was dehydrated and poorly nourished. This excess peeled skin was majorly observed on breast, abdomen, and thighs and over the head. If we observe in most of the cases with TEN, patient become dehydrated because of detachment of epidermal cells and secretions. Drugs are the most common cause accounting for about 65-80 % of the cases.¹ An immune mechanism is implicated in the pathogenesis but its nature is still unclear. It is primarily directed at drug modified epidermal cells.⁹ In this report patient was earlier diagnosed with convulsions and on treatment with Phenytoin 100 mg x 2/day for 45 days. On the 46th day patient had her 91 dose on morning after breakfast 9AM within 4hours she developed severe rashes and blisters all over the body, than the patient parents thought it was a chicken pox and they went for superstitious treatment for one week and she left her medication during the superstitious treatment. Patient again develops seizures of one episode than she restarted her medication of one dose, very rap-



Figure 1: Before treatment, toxic epidermal necrolysis due to phenytoin



Figure 2: XAfter treatment

idly she regains the blister formation on the skin, severe rashes all over the body and skin becomes scaly, black and peeled out as sheets.

As a rule oral, genital and anal mucous membranes are severely involved. Nail shedding and hair loss may occur. Mucous membrane involvement occurs in 85–95% cases and precedes the skin involvement in one third of cases.⁹ the following patient mucous membranes of mouth, genital were severely affected peeled out scaly skin and mucous secretions leads to blockage of cavities and hair loss was also observed. Causality assessment of the event with Naranjo' scale suggest "Probable".

The following diagnostic criteria must be fulfilled for a case to be labelled as toxic epidermal necrolysis.

1. Bullae or erosions involving more than 20% of body surface area or three different anatomical sites.
2. Skin peeling in sheets of more than 3 cm.
3. Involvement of non-exposed skin.
4. Mucous membranes frequently involved.
5. Skin tenderness within 48 hours of rash.
6. Biopsy confirmation within 48 hours.
7. Fever.
8. Bullae arising on an erythematous background.
9. Exclusion of Staphylococcal scalded skin syndrome.

Investigations usually show leukocytosis, albuminuria, water and electrolyte imbalance and raised transaminases.¹In the past 20 years, isolated cases of TEN-SJS have been reported in patients with brain tumors (primary or metastatic) soon after receiving cranial radiotherapy while on treatment with anticonvulsants, particularly phenytoin.¹⁰

Although the pathogenesis of these lesions is unknown, a number of hypotheses have been put forward.¹¹Treatment is mainly supportive with removal of the precipitating agent, good nursing care preferably on a ripple bed, care of the eyes and mouth to prevent scarring and infection and maintenance of fluid and electrolyte balance. Intravenous fluids were given for three days. Intravenous fluids should be supplemented with potassium. Patient was prescribed anti-bacterial Injection ceftriaxone of 1gm through intravenously for three days to prevent the further infections, Inj. Chlorpheniramine maleate intravenously thrice a day for three days, Inj. Dexamethasone intravenously thrice a day for three days, this anti-histamine and corticosteroid were prescribed to reduce the hypersensitivity reactions because of her severity is more. The patient should be put on a high protein diet. At least 2000 cal should be given during the first 24 hours increasing by

500 cal/day up to a maximum of 4000 cal/day. After five days patient was recovered, her medication was altered. She was well counselled by the pharmacists and provided red alert card of drug phenytoin with doctor suggestions through department of pharmacy practice.

CONCLUSION

Toxic epidermal necrolysis is a severe life threatening complication associated with use of anticonvulsants like phenytoin which may have familial tendency. Moreover, proper counselling to the patient regarding the use of medications is of utmost importance, in such life threatening conditions where treatment guidelines remain hazy. It is also advisable to give personal "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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