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Phenytoin-Induced Toxic Epidermal Necrolysis: A Case Report

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ABSTRACT: Toxic epidermal necrolysis(TEN) is a potentially life threatening mucocutaneous reaction usually associated with certain drugs such as; antiepileptic in which Phenytoin being the most common cause for TEN. Here we are going to present a case of 18 years old female, who presented with skin erosions associated with bullae, she also showed Direct Nikolsky sign positive and she was on anti-epileptic agents (Levetiracetam, Phenytoin) for her past epilepsy. By analysing the subjective, objective evidencethe patient was diagnosed as Phenytoin-induced TEN; which was confirmed by using WHO UM causality scale, NARANJO scale, ALDEN & SCORTEN score.

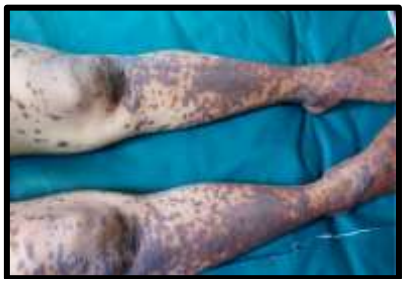
KEYWORDS: Toxic Epidermal Necrolysis, Phenytoin, Nikolsky sign, Anti-epileptic.

I. INTRODUCTION

Toxic epidermal necrolysis also known as Lyell's syndrome is a rare but potentially life threatening condition, affecting approximately 1 or 2/1,00,000 annually[4]**.** It is characterized by dermoepidermal detachment [1]. 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)[4]. It is a drug-induced reaction and the most common causative agents include sulfonamides, barbiturates, pyrazolones, and antiepileptic [1]. Phenytoin constitutes 13.37% of the documented drug-induced SJS-TEN cases [2]. Phenytoin is a widely used medication for common types of epileptic seizures. Time taken for phenytoin induced cutaneous rashes can be between 2 and 8 weeks after initiation of treatment and may progress despite discontinuation of the drug. Withdrawal of the causative drug and supportive care are the cornerstone of management of TEN. Various immunomodulatory treatments for SJS and TEN have been proposed, such as glucocorticoids, intravenous immunoglobulins (IVIG) and cyclosporine [3]. We hereby present a 18 years old female who developed TEN as a result of phenytoin which was prescribed to her for seizures due to road accident.

II. CASE PRESENTATION

A 18years old female patient was admitted to hospital with chief complains of itchy skin lesion over the body since 3days, patient was also having an episode of fever before 1day, following which develop itching skin lesion and bullae with sudden onset rapidly progressive in nature, which start over upper limb to trunk, abdomen, chest and to face. Patient was having a history of road traffic accident 20 days back and was attacked with epilepsy, for which she was on T. Phenytoin 100mg TID, T. Levetiracetam 500mg BD, T. Acetaminophen 650mg SOS. On examination, patient was febrile, BP was 110/80mmof Hg, pulse 82bpm, Spo2 98%. On skin examination by dermatologist, multiple purpura were present over B/L upper limb, chest, abdomen, trunk, neck, face, B/L over forearms and back of trunk. On oral cavity examination, it shows few erosions over the hard palate with whitish plaque +ve and direct nikolsky test was +ve.



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On this bases the dermatologist diagnosed it as Toxic epidermal necrolysis, and recommended to stop the past medication which were taken by the patient, and advised T. Chlorpheniramine 10mg IV once A Day, Framycetin cream twice a day, and Calamine lotion twice a day. On laboratory investigation the abnormal values were Hb 11.7g/dl, AST 89U/L, ALT 94U/L and Serum. Creatinine 59mg/dl. Patient was shifted to emergency ward and started Inj. Dexamethasone 8mg IM for first 4days followed by 4mg for next 4 days. Patient was on IV Fluids 1pint DNS on maintenance dose for 3days, Povidone iodine gargle 10ml for 4times a day, saline nasal drops 3drops each over TID. On 6th day lab investigations were repeated, all the values were in normal range. On 8th day patient was discharged and advised to take T. Prednisolone 30mg for first 5days, then20mg for next 5days, and 10mg for last 5days, T. Ranitidine150mg OD for 15days, T. Cetirizine 10mg OD for 5days and Framycetin cream to be continued.

This case was analysed by using WHO-UM Causality scale, Naranjo scale, ALDEN and SCORTEN scale. According to ALDEN scale Phenytoin scored 6 which is 'very probable' and Levetiracetam was 5 'probable'. From this, the drug which is more prone to cause TEN is Phenytoin than levetiracetam. According to WHO-UM causality scale patient fall under 'Certain' and total score of Naranjo scale algorithm was 7 which is categorised as 'probable' reaction. SCORTEN scale total score was 2 (i.e. 12% mortality). On the bases of all this scale it was concluded as phenytoin induced Toxic epidermal necrolysis.

III. DISCUSSION

Toxic epidermal necrolysis (TEN) is a rare, potential life-threatening dermatological condition that is usually induced by a reaction to medications such as sulfonamides, barbiturates, pyrazolones, and antiepileptics. Antiepileptic medicines such phenytoin, carbamazepine, and phenobarbital have been classified as high-risk for inducing TEN.

It is characterized by rapidly developing extensive erythema, necrosis, and detachment of the epidermis and mucous membranes that result in severe complications[1].

TEN is a rare severe mucocutaneous drug reaction which is also known as Lyell's syndromewas first described by Lyell in 1956. It is a part of spectrum of dermatological condition involving three variants as per the body surface area. If BSA less than 10% its SJS ,10-30% BSA it is considered as SJS–TEN overlap syndrome and more than 30% BSA is indicated as TEN. TEN is a rare with an incidence rate of 0.4-1.2 per million individuals[2].

The major causative drugs that were responsible for causing such mucocutaneous reactions are antimicrobials (37.27%), antiepileptics (35.73%) and non-steroidal anti-inflammatory drugs (15.93%), carbamazepine (18.25%), phenytoin (13.37%), fluoroquinolones (8.48%) and paracetamol (6.17%)[3].

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

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

Investigations usually show leukocytosis, albuminuria, water and electrolyte imbalance and raised transaminases [4].

In current case patient developed episodes of fever before 1day,following which develop itching skin lesion and bullae. Multiple purpura present over B/L upper limb, chest, abdomen, trunk, neck, face B/L lowerlimb. Few flaccid bullaes seen over B/L forarm, back of trunk.
Oral cavity; few erosion over hard palate with whitish plaque+ ,Direct nikolsky +ve. Here patient was on Tab. Phenytoin 100mg 1-1-1, Tab. Levetiracetam 100mg 1-0-0 & Tab. Acetaminophen 500mg SOS since 20days back.

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In current case suspected causative drug phenytoin was immediately withdrawn and patient was managed symptomatically with supportive careand the following therapy was added dexamethasone, iv fluids, chlorpheniramine, framycetin cream, acetaminophen, calamine lotion, salt water gargle, povidone iodine gargle, saline nasal drop. then patient had discharged with following medications tab. prednisolone, tab. ranitidine, tab. cetrizine & framycetin cream.

In this study the toxic epidermal necrolysis was analyzed by using the WHO-UM causality scale, Naranjo scale, ALDEN and SCROTEN scale. According to the WHO-UM causality scale the patient falls under the certain category and total score of the Naranjo scale algorithm was 7 which is categorized as probable reaction.

Then ALDEN score for Phenytoin was 6 & Levetiracetam was 5.

Then SCROTEN total score was 2 (ie., 12% mortality).The offending drug was dechallenged, as rechallenge was risky for the patient condition.

IV. CONCLUSION

In our case, we found that the Phenytoin was a sole reason for occurance of TEN. The patient was prescribed with phenytoin for her seizures condition, she or her family members should have been enlightenedabout early symptoms of SJS/TEN which will help physicians to detect culprit drug and discontinue its use so that impending severity of ADR is either prevented or reduced and expected morbidity or mortality is hampered.

PATIENT PERSPECTIVE

Initially during admission the patient was depressed about her condition. Later, after the start of the treatment, which was yielding good results the patient started to grew positively, and showed remarkable change both physically and mentally we humbly thank the medical teams for helping her to recover.

CONSENT OF THE PATIENT

Written informed consent was obtained from the patients for publications of this case report and accompanying images.

AUTHOR AGREEMENT STATEMENT

This is an original work done and we solemnly declare that the manuscript has not been published before in any other journals. We also confirm that all the mentioned authors are aware of all the declarations and agree to them.

Declaration Of Competing Interest

No conflicts of interest.

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