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A PHENYTOIN INDUCED TOXIC EPIDERMAL NECROLYSIS (TEN) - A CASE REPORT

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ABSTRACT

Introduction: Toxic Epidermal Necrolysis (TEN) is a rare, potentially life threatening dermatological condition that is usually induced by medications. The usage of anticonvulsants like carbamazepine, phenytoin, lamotrigine, phenobarbital, fosphenytoin are associated with high risk for occurrence of TEN. **Case Report**: A 30 year old male patient was admitted in dermatology department in a tertiary care hospital with chief complaints of rashes all over body, maculopapular rash along vesicles, throat pain, dysphagia. patient has a history of use of Phenytoin 300mg/day, 100mg in the morning and 200mg at night for his generalized tonic-clonic seizure disorder for a period of 15 days. Patient was asymptomatic 10 days back but later developed maculopapular rash **Discussion:** Based on physical examination and clinical symptoms patient was diagnosed as phenytoin induced toxic epidermal necrolysis. After having a conformational diagnosis the offending drug(phenytoin) was stopped and prescribed T. Levipil (500mg/ BD), T.Clobazam(10 mg/BD) for seizures. For symptomatic management of the condition patient was treated with dexamethasone (4mg/day) for a period of 7 days and then gradually tapered off, pheniramine malate (2mg/day) for 5 days, soframycin for local application twice daily, Tears plus eye drops was given for conjunctival lesions. Skin lesions started healing within a couple of weeks. Rashes resolved in 45 day. **Conclusion:** Early

identification and withdrawal of offending (causative) drug and rapid initiation of supportive care is the mainstay for the management of (TEN).

KEYWORDS: Toxic epidermal necrolysis, phenytoin, tonic-clonic seizures, maculopapular rash.

INTRODUCTION

Toxic epidermal necrolysis (TEN) also known as Lyell's syndrome was first described by Lyell in 1956.TEN can be defined as rapidly developing extensive erythema, necrosis, and detachment of the epidermis and mucous membranes that result in severe and fatal systemic complications such as sepsis if left untreated.[1] The word toxic alludes to the constitutional symptoms while necrolysis refers to the necrosis and detachment of the full thickness of the epidermis.[2] The affected skin may develop flaccid bullae and may detach irregularly, sometimes in large sheets with just a sliding touch (Nikolsky's sign).[3] TEN is commonly considered a drug-induced reaction rather than a skin disease; the most common causative agents include sulfonamides, barbiturates, pyrazolones, and antiepileptics. Other causes are dehydration, increased energy expenditure and local or systemic infection such as septicaemia Cases with epidermal detachment involving <10% of body surface area (BSA) are considered Stevens–Johnson syndrome (SJS) while those with 30% or more are labeled TEN. The SJS-TEN overlap is an intermediate condition where skin detachment involves 10-30% of BSA. SJS and TEN are reported as related manifestations of the same patho mechanism with different grades of severity of epidermal necrosis.[4] SJS and TEN are severe and life-threatening conditions with mortality rates of 1–5% and 25–35%, respectively.[5] More than 90% of SJS and TEN cases occurred in the first 63 days of anti- epileptic drug use.[6] Incidence rate of Phenytoin induced mucocutaneos reactions is 13.37% in India.

CASE REPORT

A 30 year old male patient was admitted in dermatology department in a tertiary care hospital with chief complaints of rashes all over body, maculopapular rash along vesicles, throat pain, dysphagia. The patient has a history of use of Phenytoin 300mg/day, 100mg in the morning and 200mg at night for his generalized tonic-clonic seizure disorder for a period of 15 days. Patient was asymptomatic 10 days back but later developed maculopapular rash. On the day of admission the patient was conscious, oriented and afebrile and his blood pressure was 110/70 mmHg. Upon physical examination, the patient showed the widespread of

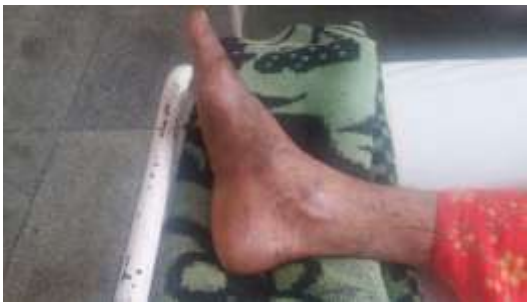
mucocutaneos rashes all over the body. The suspected drug, phenytoin was advised to discontinue, and was kept under observation.

Laboratory Investigation: Laboratory investigations revealed decrease in hemoglobin i.e.10.2gm% (13 – 16gm %) and white blood cell count of 2,500/mm3(4,500 and 10,000 cells/mm$^{3)}$, platelet count was found adequate, an erythrocyte sedimentation rate of 68 mm/ after first hour(0-22 mm/hr). Based on patients clinical symptoms he was diagnosed as Phenytoin induced Toxic epidermal necrolysis.

Treatment

For seizures: T. Levipil (500mg/ BD), T.Clobazam(10 mg/BD) was prescribed and Phenytoin was stopped, for symptomatic management of the condition patient was treated with Intravenous fluids for three days, dexamethasone (4mg/day) for a period of 3 days and then gradually tapered off, pheniramine malate (2mg/day) for 5 days, soframycin for local application twice daily, Tears plus eye drops was given for conjunctival lesions. Skin lesions started healing within a couple of weeks. On discharge, patient's condition was significantly improved. Rashes resolved in 45 days.

Following is the figure of patient showing erosions of epidermal and mucous membrane



DISCUSSION

- TEN and SJS are related mucocutaneous disorders with an estimated incidence of 0.4–1.2 patients per year.[7]
- Overall mortality for SJS ranges from 5% to 25%, and that for TEN ranges from 15% to 40%.
- 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 all over the body.
- On physical examination patient was dehydrated and poorly nourished. If we observe in most of the cases with TEN, patient become dehydrated because of detachment of epidermal cells and secretions.
- Drugs account for 65-80% of the cases. An immune mechanism is implicated in the pathogenesis but its nature is still unclear. Epidermal necrolysis is caused by interactions between CD95 L and Fas (CD95).[9][10] Disseminated keratinocyte death in SJS/TEN can also be due to Granulysin.[9]

- The studies performed in Taiwan indicate a strong association between HLA-B*1502 allele and phenytoin induced SJS/TEN and declared that the allele can be considered as a universal marker for phenytoin induced TEN, which is not supported by few studies.[11]
- Treatment is mainly supportive with removal of the precipitating agent, good nursing care, 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 also prescribed Inj. Chlorpheniramine maleate intravenously twice a day for five days, Inj. Dexamethasone intravenously twice a day for three days and next four days dose of dexamathasone was gradually tapered off, this anti-histamine and corticosteroid were prescribed to reduce the hypersensitivity reactions because his severity is more.
- The patient should be put on a high protein diet.
- After seven days patient recovered, his medication was altered
- Topiramate or Levetiracetam (antiepileptic drugs) will be the treatment of choice for this patients when phenytoin or carbamazepine has induced TEN.
- Patient was well counselled by the pharmacists of drug phenytoin with doctors suggestions.
- Regular monitoring of such ADRs, educating physicians and patients can help in early diagnosis and prevent the development of serious consequences of this idiosyncratic reaction.

CONCLUSION

Toxic epidermal necrolysis being a severe and rare life threatening complication associated with use of anticonvulsants like phenytion. Physicians and Pharmacist should counsel patients on the importance of notifying their physician if they develop any new or unusual symptoms and patient should be provided with 'drug alert card' and advised to carry it with them whenever they seek medical attention.

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