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Case Report

Carbamazepine induced toxic epidermal necrolysis in a patient of seizure disorder

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ABSTRACT

Toxic epidermal necrolysis (TEN), also known as Lyell's syndrome, is a widespread life-threatening mucocutaneous disease where there is extensive detachment of the skin and mucous membrane. Many factors are involved in the aetiology of TEN, the most common being the adverse drug reactions. Here we report a case of TEN in a 12 year old female child who presented with fever and blisters all over her body after taking carbamazepine for uncontrolled generalised tonic-clonic seizure. This case has been reported to highlight the importance of using carbamazepine cautiously as this case shows the "probable" association between carbamazepine and TEN, which is a life threatening condition.

Keywords: Carbamazepine, TEN, SJS, Generalised tonic –clonic seizure

INTRODUCTION

Adverse drug reactions form 2-3 % of the hospitalized patients. The percentage of potentially serious reactions is around 2 %. Stevenss-Johnson syndrome (SJS) and TEN are potentially serious cutaneous reactions characterized by high fever, widespread blistering exanthema of macule and atypical target-like lesions accompanied by mucosal involvement.[1] Anticonvulsants are one of the main triggers, causing SJS/TEN, and among anticonvulsants carbamazepine is responsible for a maximum number of cases.[2] Clinically, TEN present as erythema, necrosis and extensive sloughing of the epidermis; mucous membrane and with symptoms of systemic involvement. Theories proposing the pathogenesis probably attribute it to immunologic reactions, reactive metabolite from certain drugs and genetic aspects.[3]

Carbamazepine is an iminodibenzyl drug initially introduced as an anticonvulsant. It is now widely used to treat seizure disorder, bipolar disorder, trigeminal neuralgia and chronic pain. Carbamazepine causes TEN in a frequency of 0.05-2 persons per million populations per year.[1,4]

This is a case of Toxic Epidermal Necrolysis in a female patient who received carbamazepine for uncontrolled generalised tonic-clonic seizure.

CASE REPORT

A 12 year old female child was admitted to paediatric ward of our tertiary care hospital with chief complaints of fever and rash since 3 days. Patient was a known case of generalised tonic-clonic seizure under sodium valproate

prophylaxis since 2 years. Due to uncontrolled seizure patient was prescribed tablet carbamazepine 200mg by a private doctor. After taking carbamazepine for 1 week she developed fever and blisters all over her body.

On admission to our hospital patient was febrile, vitals were stable and pallor was present. Local examination showed blisters with generalized hyperpigmented necrotic lesion all over the body including palms, soles with erosions over the mucosal membrane along with fissuring of lips (Figure 1).

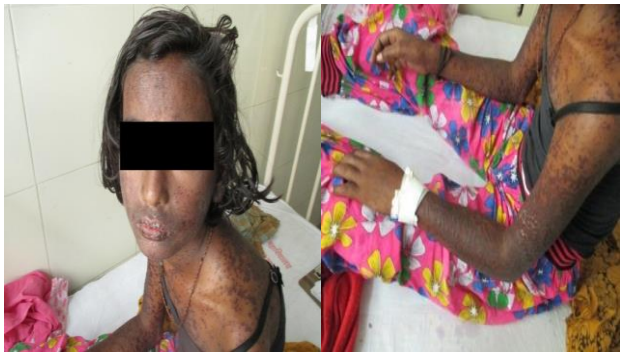

Figure 1: Generalised hyperpigmented patches and blisters on admission.

Blood investigation showed moderate anaemia (8.2gm %), liver function test, serum electrolyte and rest of complete blood count parameters were normal.

As per Bastuji Garin classification the diagnosis was toxic epidermal necrolysis with spots.[5] Carbamazepine was the suspected drug which was withdrawn. Patient was given supportive treatment with injection cefotaxime and injection hydrocortisone.

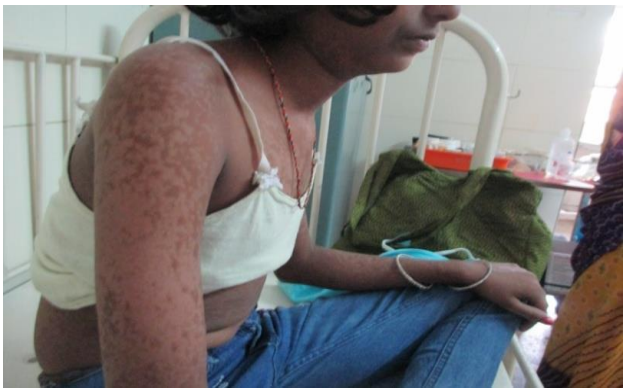

Figure 2: Healed hypopigmented macules during discharge.

Patient improved with the treatment and was discharged with follow up after 1 week. On follow up patient had only few hypopigmented patches and oral ulcers (Figure 2). Patient was advised to continue tablet sodium valproate 200mg once daily.

DISCUSSION

SJS and TEN are severe idiosyncratic reactions characterized by fever and mucocutaneous lesions leading to necrosis and sloughing of the epidermis. Depending upon the body surface area (BSA) involved, three entities are recognized.

- SJS: A minor form of TEN, with <10% BSA involvement
- Overlapping SJS/TEN: Ten to thirty percent of the BSA
- TEN: More than 30% of the BSA involved.[6]

Although SJS/TEN has multiple etiologies and commonly triggered by viral infections (herpes simplex virus) and neoplasias however, the most common cause is the use of medications. Among the drug mostly implicated are allopurinol, antibiotics, anticonvulsants, and non-steroidal anti-inflammatory drugs. Recently, in a seven year study Devi, et al concluded that anticonvulsant were the main drug responsible for SJS especially in the first eight weeks of treatment, and the main drug responsible was carbamazepine (more than 80%). The increases number of prescriptions of carbamazepine for the control of pain may be the reason for the increased frequency of SJS/TEN to carbamazepine.[2]

The mechanism of SJS/TEN is not well understood. An idiosyncratic, delayed hypersensitivity reaction has been implicated in the pathophysiology of SJS/TEN. Association with HLAB* 1502 and HLAB15 has also been seen in East Asian population.[7] The average reported mortality rate of is 25-35% and sepsis is the main cause of death.

The patients usually develop hypersensitivity reaction to the drug carbamazepine between 2 and 12 weeks.[8] Our patient presented with generalized peeling of the skin with mucosal ulceration after a week of initiating the therapy with carbamazepine. As per the Roujeau and Stern algorithm for implicating a drug as the cause of an adverse drug reaction, alternative causes such as infections were ruled out, the time of onset of the starting the medication was less than 3 weeks.[4] Patient improved after withdrawal of carbamazepine. Reinstitution of the other drugs especially, sodium valproate did not produce any adverse reactions. Hence by exclusion, carbamazepine was the causative agent for producing TEN. Read ministration of the offending drug was not resorted because there are reports of fatalities. The main therapeutic action in TEN is early reorganization of the drug reaction and withdrawal of the drug, there is no universally accepted, definitively effective, specific treatment for the SJS/TEN other than supportive care. Glucocorticoid is useful only in early stage of the disease.[7] In our case rapid withdrawal of the offending drug carbamazepine and supportive treatment lead to rapid cure of the patient.

In the present case, the causality is "probable" to the drug carbamazepine in both Naranjo probability assessment scale with score of 6 and World Health Organization causality assessment scale.[9,10] ALDEN alogarithm which is a specific causality assessment algotithm for SJS/TEN, shows that the ADR is very probable with score of 6.[11] The ADR was of moderate severity of level 4 as per the Hartwig's Severity Assessment Scale and was probably preventable according to Modified Schumock and Thronton criteria for preventability of ADR.[12,13]

CONCLUSION

In the view of the increase in the number of prescriptions for carbamazepine in recent years, "probable" association between carbamazepine and TEN in this case report and the seriousness of the adverse drug reaction, this case has been reported to highlight the importance of using carbamazepine cautiously keeping in mind its association with TEN as it is a life threatening condition.

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