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Case Report

Pharmacology Section

Can Vitamin B-Complex Aggravate the Carbamazepine Induced Toxic Epidermal Necrolysis?

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ABSTRACT

Toxic Epidermal Necrolysis (TEN), which is also known as Lyell's syndrome, is a widespread, life-threatening, mucocutaneous disease that is particularly observed secondary to drug-taking and less commonly secondary to infections and immunization. Carbamazepine is associated with benign pruritic rash in 10-15% of the patients, but the life threatening dermatological syndromes like exfoliative dermatitis, erythema multiforme, the Stevens-Johnson Syndrome (SJS) and TEN are rarely seen with the carbamazepine treatment. The 32 year old female suffering from chronic backache, who was prescribed carbamazepine along with an intravenous combination of vitamin B-complex and calcium, developed fever, cough and mucocutaneous manifestations of TEN after 15 days of the treatment. She was treated in the hospital with systemic steroids, intravenous immunoglobulins, antibiotics, intravenous fluids and supportive care. In spite of the above treatment, the patient could not survive for more than seven days.

Key Words: Toxic epidermal necrolysis, Carbamazepine, Drug reaction, Systemic steroids

INTRODUCTION

Toxic Epidermal Necrolysis (TEN) is the severe form of the Stevens-Johnson Syndrome (SJS). Alan Lyell described four patients of TEN for the first time in 1956 [1]. The consensus classification of acute bullous disorders [2]defined SJS as an epidermal detachment below 10% of the body surface area with widespread erythematous or purpuric macules or flat atypical targets and TEN as an epidermal detachment above 30% of the body surface area, whereas the involvement of 10-30% of the body surface area is defined as a SJS-TEN overlap.

Drugs are responsible for more than 50% of the cases of SJS and for almost 80-95% of the TEN cases. Infections and immunizations are the other rare causes of SJS/TEN. More than 100 drugs have been implicated to cause SJS/TEN. Sulfonamides, NSAIDs and anticonvulsants have been cited as most common in most of the surveys and reviews [3]. Among all the anticonvulsants, carbamazepine is the most common cause of TEN. Carbamazepine is an iminodibenzyl drug which is used for the treatment of epilepsy, trigeminal and glossopharyngeal neuralgias and bipolar affective disorders. There is a significant association between the HLA-B*1502 allele and the risk of developing Carbamazepine induced SJS/TEN [4].

Here, we are reporting a case of 32 year old female patient who developed TEN with carbamazepine use.

CASE REPORT

A 32 year old female with the complaints of oral lesions with a difficulty in swallowing and skin lesions, was admitted to the Department of Skin and Venereal Diseases of Goa Medical College and Hospital on 28th April, 2012.

The patient was suffering from backache since 2 ½ years, which had increased in severity in association with the headache since the past 20 days. The patient went to a private clinic with these complaints and was prescribed Tablet carbamazepine (200 mg twice daily) and Tablet fexofenadine. Nine days later, she was given three injections of a combination of vitamin B1, B6, B12 and calcium intravenously on alternate days.

Fifteen days later i.e. after the third dose of the combination of vitamin B1, B6, B12 and calcium, the patient developed oral ulcerations with a difficulty in swallowing and a burning sensation in the mouth along with fever and cough. It was associated with redness and a watery discharge from both the eyes with severe itching.

Two days later, she developed fluid filled skin lesions which were suggestive of vesicles and bullae over the trunk, back, and bilaterally on the upper limbs. On the same day, she was admitted in the private hospital, where she was given a course of antibiotics and steroids (methylprednisolone). No improvement was seen in spite of this treatment. In fact, the patient continued to develop new lesions. The patient was shifted to our hospital after three days of treatment in the private hospital. The previous vesicles and bullae became tense and they increased in size and coalesced each other. The medical history was not significant. The personal history was not remarkable, except for the disturbed sleep.

The dermatological examination on admission revealed a generalized, bilateral and an asymmetrical involvement of the body, which included the orogenital mucosa in the form of vesicles, bullae and erosions, with the peeling of the skin over the trunk, back and the buttocks [Table/Fig-1]. On systemic examination, the patient was found to be conscious, oriented and febrile (low grade). Her blood pressure was 124/80 mm of Hg and her pulse was 110/min. The patient was administered teicoplanin (800mg IV stat), piperacillin + tazobactam (4.5 gm 8 hourly), aztreonam (1 g 12 hourly), metronidazole (500 mg 8 hourly), pantoprazole,

[Table/Fig-1]: Skin lesions seen in patient

ondansetron, pheniramine, clotrimazole mouth paint, ciprofloxacin eye drops and fusidic acid cream. She received intravenous immunoglobulins in a dose of 0.4 g/kg body weight.

She expired after 7 days due to a septicaemic shock.

DISCUSSION

Drugs frequently cause adverse cutaneous reactions which affect 2-3% of all the hospitalized patients. The average incidences of SJS and TEN are estimated at 1.2 to 6 and at 0.4 to 1.2 cases per million, per year respectively. An early diagnosis, the withdrawal of suspected drugs and a proper management may improve the prognosis of SJS and TEN [5]. Females are affected more commonly than males in the ratio of 1.5:1 and this ratio increases with age [6]. The disorder is more likely to affect the people who suffer from the SLE and the HIV infections [7]. A study which was done by Kaur et al., [8] showed a peak incidence of TEN in the fourth and sixth decades of life.

In our patient, the alternative causes of TEN such as infections and immunizations were ruled out. The adverse reactions started 15 days after the initiation of the suspected drug administration. Carbamazepine is a well known cause of TEN. After applying the Karch and Lasagna algorithm, the causation was listed as probable in our case.

The TEN patients should be treated in the burns unit with appropriate care and nursing, like the protection of the cutaneous and the mucosal surfaces which are involved, monitoring of the electrolytic balance, fluid replacement, nutritional support, adequate care of the eyes and the prevention and the treatment of the infection. The role of steroids was a debatable issue till now. Some studies have shown it to be useful [9], while others have shown it to be detrimental [10]. A study which was done by Schneck et al concluded that corticosteroids did not show a significant effect on the mortality in comparison with the supportive care only [11]. A retrospective monocentre study which was done by Kardaun SH and Jonkman MF suggested that a short course pulse of high dose steroids (dexamethasone) may be beneficial in these patients [12]. In our case, the patient did not improve after the steroid therapy; in fact, she continued to worsen even after the administration of steroids. A dramatic improvement has been reported with intravenous immunoglobulins (IVIg) in a dose of 0.2 to 0.75 g/kg body weight when they were administered within 72 hours of the onset of the symptoms. However, no randomized clinical trials have been published till now. Our patient received IVIg after 72 hours of the onset of the symptoms. Morever, our patient received intravenous injections of vitamin B-complex and a calcium combination, which were known to produce hypersensitivity reactions. So, does the concurrent administration of the intravenous vitamin B complex-calcium combination with carbamazepine/offending drug aggravate the drug induced SJS/TEN? This needs to be investigated in detail.

Carbamazepine is being increasingly used for the treatment of epilepsy, neuralgias and bipolar disorders. It is not possible to predict the risk of developing SJS/TEN in every patient, but some studies have shown that the genetic tests for HLA-B* 1502 and a patch test could be useful in detecting the high risk patients [13,14].

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