

Carbamazepine Induced Generalised Erythematous Rash in a Patient of Bipolar Affective Disorder - Case Report

Pohane P*, Jaiswal S, Chandurkar A, Sawant V and Vahia VN

Department of Psychiatry, HBT Medical College and Dr. R. N. Cooper Municipal General Hospital, Mumbai, India

Introduction

Carbamazepine is primarily used as an anticonvulsant in the treatment of grand mal and focal seizures. Other indications for its use include trigeminal neuralgia, bipolar affective disorder and some off label uses in psychiatry such as impulsive behaviour, disruptive behaviour, substance use disorders to name a few [1-3]. Mood disorders are a group of clinical conditions characterized by a loss of the sense of control and a subjective experience of great distress. Patients with elevated mood demonstrate expansiveness, flight of ideas, decreased sleep, and grandiose ideas. Patients with depressed mood experience a loss of energy and interest, feelings of guilt, difficulty in concentrating, loss of appetite, and thoughts of death or suicide. Other signs and symptoms of mood disorders include change in activity level, cognitive abilities, speech, and vegetative functions (e.g., sleep, appetite, sexual activity, and other biological rhythms). These disorders virtually always result in impaired interpersonal, social, and occupational functioning [4].

The common side-effects associated with carbamazepine therapy are dizziness, diplopia, drowsiness, ataxia, nausea and headaches dry mouth, oedema, hyponatraemia and sexual dysfunction. They can sometimes be avoided by starting with a low dose and increasing slowly, avoiding high peak blood levels by splitting the dose throughout the day, or using a controlled release formulation, may also help [5].

Around 3 percent of patients treated with carbamazepine develop a generalised erythematous rash, serious exfoliative dermatological reaction can rarely occur [6].

Case Report

Miss T. S. 19 years old unmarried female of lower socioeconomic strata presented to outpatient department with complaints of excessive talkativeness, tall claims, irritability and disturbed biological functions for 3 months.

Patient had history of irritability, excessive talking, and making tall claims about having lot of money. There was history of excessive grooming and hypersexuality, she would ask strangers for sexual favour and would go along with them for 1-2 days. Along with these, she had disturbed biological functions such as decreased need for sleep and no treatment was sought for 3 months.

Before this episode she had two episodes of similar complaints in last 2 years. Each episode was lasted for 3-4 months period and treated with drugs, details of which are not available. The medications were discontinued soon after she got better by her. In between these two episodes she had one episode of low mood, suicidal ideation, loss of interest at work and disturbed biological functions, which lasted for 5-6 months and no medical attention was received for this episode.

With this patient was presented to outpatient department. She was physically within normal limits. Family and personal history was not contributory. On mental status examination positive findings were

increased motor behaviour, increased productivity of speech, euphoric affect, delusion of grandeur, impaired judgement, and had grade one insight. She was diagnosed as Bipolar affective disorder, current episode manic with psychotic symptoms (ICD10: F31.2), and admitted to psychiatry ward for further management. Her score on Young Mania Ratings Scale was 43 at the time of admission.

She was assessed on baseline for laboratory investigations which were essentially unremarkable; she was started on Tablet carbamazepine and Tab. Olanzapine as it was best available option considering her reproductive age group and availability of medicine on hospital schedule. Tablet carbamazepine was gradually hiked to 1000 mg with serum level monitoring and olanzapine was hiked to 20 mg. Patient achieved remission within 8-9 days with YMRS score 7. After 7 days maintaining on 1000 mg of Tablet Carbamazepine (serum carbamazepine- 14 mg/ml) patient had maculopapular rash all over the body. Rash were not photosensitive and were present all over body including exposed as well as non-exposed body parts. There were no other physical findings such as lymphadenopathies, arthralgia, osteonecrosis and myopathy which are common in systemic lupus erythematosus present. Her systemic examination was within normal limits.

Maculopapular rash were disappeared gradually after omission of carbamazepine within 5 days with additional treatment of Tablet Prednisolone 40 mg which tapered gradually. After the rash disappeared patient was reintroduced to olanzapine and lithium was started in place of Carbamazepine (Figure 1).

Discussion

Although maculopapular rash, Toxic epidermal necrolysis have 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 TEN/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 [7].

*Corresponding author: Pohane P, Department o of Psychiatry, HBT Medical College and Dr. R. N. Cooper Municipal General Hospital, Mumbai, India, Tel: 022 2620 7257; E-mail: pohanepranav@gmail.com

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Figure 1: A generalised erythematous rash due to carbamazepine drug eruption.

The mechanism of carbamazepine induced cutaneous reactions is not well understood. An idiosyncratic, delayed hypersensitivity reaction has been implicated in the pathophysiology of Toxic Epidermal Necrolysis. Association with HLAB* 1502 and HLAB15 has also been seen in East Asian population [8]. The patients usually develop hypersensitivity reaction to the drug carbamazepine between 2 and 12 weeks [9]. Our patient presented with generalized erythematous rash after more than two weeks of initiating the therapy with carbamazepine. Although carbamazepine causes adverse drugs reactions in patients with certain genotype, SNPs were not tested due to cost consideration of patient. As per the Roujeau and Stern algorithm [10] for implicating a drug as the cause of an adverse drug reaction, alternative causes such as infections were ruled out and the time of onset of the starting the medication was less than 3 weeks.

Patient was improved after withdrawal of carbamazepine and reinstitution of olanzapine did not produce any adverse reactions. Hence by exclusion, carbamazepine was the causative agent for producing generalised erythematous rash. The main therapeutic action in skin rash is early recognition of the drug reaction and withdrawal of the drug. There is no universally accepted, definitively effective, specific treatment for the skin rash other than supportive care. Glucocorticoid is useful only in early stage of the disease.⁸ In our case rapid withdrawal of the offending drug carbamazepine and supportive treatment lead to rapid cure of the patient.

Conclusion

There is increase in the number of prescriptions for carbamazepine in recent years. In this case report there is the “probable” association between carbamazepine and generalised erythematous rash. This case has been reported to highlight the importance of using carbamazepine cautiously keeping in mind its association with skin rash and other serious conditions.

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