CASE

Lamotrigine induced Stevens-Johnson syndrome: a case report

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Abstract

A young female treated for manic episode with valproic acid, when later on added lamotrigine, she developed generalised body lesion and diagnosed as Stevens-Johnson syndrome.

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Introduction

Lamotrigine (LTZ) is a novel anti-epileptic of phenyltriazine class. Its mood stabilising effect was seen by Smith et al.[1] Since then many researches reestablished its efficacy in various trials.[2-6] The drug acts at voltage-sensitive sodium channels to stabilise neuronal membrane and inhibit transmitter release, principally glutamate release.[7]

Valencia et al.[8] in their study of 72 patients, found that most common adverse event with LTZ was "rash" (seven per cent) and rate of discontinuation of LTZ was around eight per cent. Incidence of rashes varies from 0.08 to three per cent, least in adults with mood disorder when LTZ was used as monotherapy and maximum with children treated with LTZ for epilepsy.[9] Another study with around 2000 subjects found that incidence of rashes in controlled setting (1056 subjects) and open-level setting (1955 subjects) were 8.3% and 13.1% respectively.[10]

Rashes usually occur in two to eight weeks of treatment initiation.[11] Rashes though most commonly are erythematous, maculopapular or morbiliform benign rashes but at times, albeit rarely can take up the life threatening form of Stevens-Johnson syndrome (SJS) or more fatal, toxic epidermal necrolysis (TEN). TEN and SJS are muco-cutaneous disorders with an estimated incidence of 0.4-1.2 patients per year.[12,13]

Perhaps the first case of death caused due to LTZ induced SJS, in India was reported by Silva Pereira et al.[14] Overall mortality for SJS ranges from five per cent to 25%, and that for TEN ranges from 15%- 40%.[12,15-18] About 90% of patient with TEN develops painful erosions in their mucosa, 85% have conjunctival lesions and about 35% of those survive experience ocular sequel.[12]

We report a case of SJS in a bipolar mood disorder patient treated with LTZ.

Case report

Miss A, 25 years old unmarried female student from semi-urban background, presented with features of bipolar affective disorder in mania without psychotic symptoms, first episode. Past and family history was not significant. Since patient's symptoms were only mild to moderate in degree, oral valproate was prescribed in 750 mg per day dosage along with zolpidem 10 mg at bed time. After two weeks, tablet LTZ 25 mg twice a day was added. After ten days, patient reported with generalised maculopapular rashes all over body for two days. Patient's look was toxic. Conjunctiva was congested, mucosal lesions were evident in the form of aphthous ulcers and thick haemorrhagic crusting of lips. Urgent dermatological referral was done and the patient was admitted in the dermatology department. A diagnosis of SJS was made. LTZ was stopped. Patient was treated with oral prednisolone 30 mg per day and tablet hydroxyzine hydrochloride 25 mg twice a day. SCORTEN[19] score was utilised for the assessment of mortality. Score of 2/7 indicated mortality rate of 12.1.

Routine investigations were done which showed anaemia (haemoglobin 9.0 gm%), leucocytosis (11,940/cmm) with neutrophilia (83.6%), random blood sugar 157 mg% and erythrocyte sedimentation rate 40 mm at the end of first hour, slight derangements of liver enzyme, with normal electrolytes (Na+ 145 meq/L; K+ 3.9 meq/L) and normal urea and creatinine. Her chest X-ray was also within normal limits.

Patient improved and discharged after two days. Patient's rashes recovered fully over next two weeks. During follow ups patient was maintained well on valproate and quetiapine. It was planned never to restart LTZ. LTZ sensitivity was explained to patient's family members.

Discussion

SJS/TEN though rare, nevertheless is a potentially fatal medical condition and needed to be managed in intensive care or burn units. It is next to impossible to predict which patient is going to develop this condition, still many things can be done to prevent occurrence of this conditions. Principles are- a) To understand what are the risk factors, b) Patient's education and c) Prompt treatment.

Risk factors:

a. Patients on certain medicines, e.g. sulfonamides, phe-

nobarbitone, carbamazepine and LTZ (high risk)[20]; nonsterooidal anti-inflammatory drugs (NSAIDS), paracetamol, valproic acid, quinolones, rifampicin, ethambutol, aminopenicillins and cephalosporins.[13]

b. Diabetic patients.

c. Acquired immunodeficiency syndrome (AIDS) patients on nevirapine.

d. Patients with epilepsy, in extremes of age.

e. High dosage and rapid titration of inflicting agents.

f. Any combination of two or more inflicting agents.

Most established association is seen with LTZ and valproic acid.[21] The latter agent strongly inhibits hepatic metabolism of LTZ, increasing its serum half-life from approximately 29 hours as monotherapy to 70 hours with valproic acid.[22]

Most reported cases of SJS or TEN due to LTZ have occurred in patients who were co-medicated with these two drugs. Wadelius et al.[23] reported three cases of TEN due to LTZ. All occurred within 14 days after LTZ was added to valproic acid.[23] Chaffin and Davis[12] reported a case of TEN after LTZ was added to carbamazepine. Bocquet et al.[24] reported two children who developed SJS when LTZ was added to valproate and clonazepam.

The prescription of LTZ should be undertaken with appropriate consideration of the potential risk of adverse events including rash to the patient in relation to potential benefit from improvement of bipolar disorder. Any combination of drugs associated with SJS/TEN should be discouraged and the benefits of such combination are to be weighed against disastrous side effects before starting therapy.

Present report calls for cautious use of LTZ in patient's already on valproic acid and highlights the importance of patient education, prompt recognition and treatment for preventing mortality and morbidity associated with serious cutaneous reactions like SJS/TEN. This case, not only impress upon an acute need for sensitising practicing psychiatrists regarding this fatal complication and how it can be prevented, but also highlights the issue of doctor-patient discussion of risk-benefit of treatment options available, keeping in mind the various lawsuits filed nowadays against medical professionals.

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