

Case Report

STEVENS-JOHNSON SYNDROME WHILE ON LAMOTRIGINE AND NSAID: A CASE REPORT

Madhavi Bhat^{1*}, Anil Kakunje¹, Rajesh Mithur¹, M Manjunath Shenoy², K A Mashood³, Sowmya Puthran¹, Anjana Joy¹

¹Department of Psychiatry, ² Department of Dermatology, ³ Department of Geriatric Medicine, Yenepoya Medical College, Yenepoya Deemed to be University, Mangalore, India

*Corresponding Address: YENCOURAGE, Dept of Psychiatry, Yenepoya Medical College, Yenepoya Deemed to be University, Mangalore. Email: madhuchethana@gmail.com

ABSTRACT

Stevens-Johnson syndrome is a severe immune-mediated cutaneous reaction occurring due to exposure to certain drugs. Lamotrigine is an FDA approved drug used in the treatment of bipolar depression. When it is given concomitantly with sodium valproate, the risk of developing Stevens-Johnson syndrome increases. Here we present the report of a patient with bipolar depression who developed serious skin rashes while on lamotrigine and NSAID prescribed by a local doctor, who recovered after timely management. This case highlights the importance of following proper dosing, drug escalation regimen and managing drug interactions during lamotrigine therapy.

Keywords: Bipolar depression, Stevens-Johnson syndrome, Lamotrigine, Sodium Valproate, NSAID

INTRODUCTION

Stevens-Johnson syndrome (SJS) is a severe immune-mediated cutaneous reaction.¹ The incidence of SJS is one to two cases per one million population.² It usually occurs due to drug reactions but can occur due to infection with *Mycoplasma pneumoniae*.¹ Allopurinol, carbamazepine, phenytoin, phenobarbital, lamotrigine, sulfonamides, nevirapine and oxycam-NSAIDs are the drugs that are highly suspected of causing SJS. Weaker association have been found for aminopenicillins, cephalosporins, paracetamol and quinolones.^{2,3}

Lamotrigine is an antiepileptic drug used in the treatment of Lennox-Gastaut syndrome, migraine, and neuropathic pain. It is an FDA approved drug for the treatment of bipolar depression in psychiatry.⁴ It acts by blocking voltage-gated sodium and calcium channels. It also has antiglutamate, antiaspartate, 5-HT3

antagonism and neuro protective action.⁵ The adverse effects commonly seen include dizziness, headache, diplopia, ataxia, nausea, amblyopia, somnolence, vomiting and rash.⁶ It is found that 0.1-1% of patients can develop severe dermatologic reactions. Lamotrigine related rash usually occurs between five days and eight weeks after drug exposure.⁷

We present an interesting case of Stevens-Johnson Syndrome (SJS) while on lamotrigine.

CASE REPORT

Written informed consent was taken for publishing and displaying the photographs of the rash without revealing the identity.

Mr X, a 57-year-old man, presented to the psychiatry department with pervasive low mood, lack of interest in

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previously pleasurable activities, easy fatigability, insomnia and reduced appetite for a month following a financial loss. He was on sodium Valproate 1000mg/day and escitalopram 10mg tablets. He was diagnosed to be having bipolar affective disorder for the past 30 years. Family members reported a history of three depressive episodes in the past following stressors, each episode lasting for two to three months. They also reported hypomanic/ manic episodes during which he used to talk more, be argumentative, and spend money unnecessarily without discussing with family members, which was not his usual self. The patient used to consume alcohol and smoke cigarettes daily in a dependence pattern for the last 10 years. The last use of the substance was one month back. He has co-morbid Type 2 diabetes mellitus and systemic hypertension, for which he is on regular treatment. The patient's elder son was diagnosed with intellectual disability during his childhood which added to his stress.

On Mental Status Examination, the patient had reduced psychomotor activity and speech. His mood was sad, and his affect was depressed. The patient had death wishes, ideas of hopelessness, helplessness, and worthlessness. The patient was admitted with the above complaints and was diagnosed to have Bipolar affective disorder- current episode severe depression without psychotic symptoms. As it was a breakthrough episode while on sodium valproate 1000 mg and was developing severe depressive episodes, he was started on Tab. Lamotrigine 25mg, which was gradually increased to 100mg over a period of five weeks. Tab Escitalopram 10mg was added in view of depression, and antihypertensives and oral hypoglycaemic agents were continued. The patient was hospitalized for six weeks and was discharged. At the time of discharge, he showed 50% improvement in his depressive symptoms as per the serial Mental Status Examination. We found that patient was taking medications regularly and was going to work.

After one month, the patient had consulted a local doctor for shoulder pain, for which he was given analgesic medications, the details of which were not available. After two days, the patient developed small red rashes over his chest and back. It spread rapidly to his extremities and face the next day. The patient had severe pain and had difficulty swallowing even liquids. The rashes involved his eyes, lips, ears and genitals too.

His skin started to peel on the second day and had even bleedings from the open skin areas. The patient had stopped taking food from the third day and could not get up from his bed. On the fourth day, the patient had confused behaviour, irrelevant talk, and disturbed sleep. For these complaints, he was brought again for admission.

Figure 1. Lesions involving face, chest, and limbs with exfoliation of the skin. The patient had difficulty opening his eyes and mouth, along with difficulty in swallowing.



Figure 2. Lesions involving the back with exfoliation of the skin.



On examination, the patient had diffuse erythematous and purpuric rashes and vesiculobullous eruptions throughout the body, involving the skin, mucous membrane, oral cavity, and genitals. Nikolsky sign was positive on examining the erythematous areas of the

skin. Skin detachment involved less than 10% of the body surface area. Emergency dermatology and physician opinion were taken. The differential diagnoses were drug hypersensitivity syndrome and erythema multiforme. These were ruled out based on history and clinical examination. Routine blood investigations were done, and they showed low haemoglobin levels and lymphopenia. CRP and ESR were found to be within normal limits, and blood culture found no growth. However, a skin biopsy was not done. After a detailed history and clinical examination, a diagnosis of Stevens-Johnson Syndrome was made. All the previous medications were stopped, and he was started on IV Dexamethasone and IV Inj Pheniramine. The patient was kept under strict isolation to prevent infections. Serum electrolytes showed hyponatremia. IV fluids were started, and the correction of sodium was initiated. Dressings with topical steroids were done in the areas with erythematous lesions. Ophthalmologist's opinion was taken to rule out any ophthalmological complications. During the hospital stay, the patient was disoriented until the correction of hyponatremia. The patient gradually improved, and the lesions started healing. The steroid was gradually tapered and stopped over seven days. He was gradually started on liquid Sodium valproate and fluoxetine in view of significant depressive symptoms. The patient improved and was discharged.

Figure 3: Healed lesions during the discharge days



DISCUSSION

We suspect the cause of SJS to be due to the adverse effect of Lamotrigine/ rapid hiking of dose in our patient. Besides, our patient was on sodium valproate, which enhances the risk of SJS. In this case, the patient had taken an unknown medication two days before the onset of rashes. Many drugs can cause SJS, including oxicam-NSAIDs.³ The patient had consulted a local doctor for shoulder pain and could have taken NSAID for the same, which could have added to the precipitation of this adverse reaction.

After the FDA approved lamotrigine for the treatment of bipolar depression, it is widely used for the treatment for the same. Clinical trials have found the incidence of rash in adults receiving lamotrigine as monotherapy to be 0.08% and 0.13% in adults receiving the drug as adjunctive therapy. It is commonly found that the risk of developing a rash increased when valproic acid is co-administered.⁸ This patient was also on sodium valproate, which is known to decrease the clearance of lamotrigine even at low doses. This leads to an increase in serum concentration of lamotrigine which in turn increases the risk of SJS.⁹ Therefore, during concomitant administration of these drugs, lamotrigine is hiked at half the usual regimen. Most cases of SJS occurred between five days and eight weeks of administration of lamotrigine.⁷ Our patient developed rashes after four weeks of administration.

Once the patient is diagnosed with SJS, the offending drug has to be stopped immediately. Providing supportive care is the most important measure. Fluid, electrolyte and temperature monitoring has to be done. Ophthalmology consultation has to be obtained to reduce long term sequelae. Analgesia has to be provided. Wet dressings with topical corticosteroids to be considered for erythematous areas. Antibiotics should be considered only if infection occurs. In severe cases, intravenous immunoglobulin (IVIg) must be administered. The use of intravenous steroids is controversial.¹

With certain precautions, severe rash associated with lamotrigine can be prevented. The most important preventive measures are appropriate dosing and dosage adjustment of the drug,⁸ unlike the case presented by Kocak et al., where the patient was on valproic acid, carbamazepine and initiated a high dose of

lamotrigine.¹⁰ This emphasizes that by following the dosing regimen, the risk of serious rash may be diminished but not eliminated. Patient psychoeducation is also important for preventing morbidity and mortality associated with serious adverse drug reaction development.⁸ Our patient recovered well due to early intervention and immediate discontinuation of lamotrigine.

CONCLUSION

Despite following an appropriate dosing regimen, SJS is an important adverse drug reaction associated with the use of lamotrigine. Hence, all patients should be monitored for the possible systemic and cutaneous adverse effect during its administration. Immediate discontinuation of the drug, monitoring for adverse effects and drug interactions and early medical intervention is important to prevent high morbidity and mortality associated with lamotrigine.

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