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Case report

Lamotrigine induced Stevens- Johnson syndrome: a case report

Nadia Afroz, Rubina Hossain, Shaafi Raaisul Mahmood, Mohammad Tariqul Alam

Abstract

Stevens-Johnson syndrome (SJS) is an immune–complex mediated hypersensitivity reaction and has been linked as an adverse reaction to many drugs that predominantly involve the skin and the mucous membranes. In most of the cases, drugs are clearly the main causative factor. Lamotrigine, an anticonvulsant is recently being used as a mood stabilizer in many psychiatric disorders. Association between SJS and lamotrigine is very rare in psychiatric settings in our country. A 19-year old female with borderline personality disorder who developed Stevens- Johnson syndrome 3 weeks after starting of lamotrigine reflect an important, but rare side effect.

Declaration of interest: *None*

Keywords: Stevens-Johnson syndrome; adverse drug reaction; hypersensitivity reaction; skin; mucous membrane

Introduction

Stevens-Johnson syndrome (SJS) is a serious disorder of the skin and mucous membrane.[1] Annual Incidence rate is 2.6 to 6.1 cases per million population and the female: male ratio is 3:2.[2] SJS is a multifactorial disorder. In 75% of the cases, drug is the main etiological factor and genetic predisposition, viral infection and idiopathic causes account for about 25% of cases.[3] This syndrome is mainly caused by hypersensitivity to certain drugs like antibiotics, NSAIDs, valproate, carbamazepine, antimalarial, sulphonamide, allopurinol, lamotrigine, etc.[1,2] In about 90% cases, there are significant involvement of the skin and mucosa of the eyes, mouth, genitalia and gastrointestinal tract manifested as erythema and erosions that is the hallmark of SJS. Lesion patterns may vary according to the severity of the condition.[1,4] Among the anticonvulsants, lamotrigine rarely causes SJS. Most common side effects of lamotrigine include headache, nausea, dizziness, diplopia and ataxia. Adverse skin reactions occur in 8.3% of patients taking lamotrigine and only 0.04% develop SJS.[5] Here we are presenting a case, where a patient developed SJS after 3 weeks of use of lamotrigine but her initial response to treatment was good and did not show any sign of the syndrome.

Case Report

A 19-year-old girl got admitted to National Institute of Mental health (NIMH) with the complaints of difficulty in controlling anger, emotional instability, unstable interpersonal relationships and history of suicide attempts several times in the last 7 years. The history revealed that she was undergoing regular follow up in a psychiatric OPD for the last 4 years and was receiving sertraline 50 mg and lithium carbonate 400 mg. She had two inpatient hospital admissions after attempting suicide on two occasions in this period of time. Along with drug treatment she also received Dialectical Behavioral Therapy. Initially her response to treatment was satisfactory, but due to discontinuation of treatment, readmission was required. After readmission, lithium was continued but response was poor. As a result lithium was stopped and lamotrigine 50 mg was started in divided doses, then gradually increased the dose to100 mg, along with an antidepressant and an antipsychotic. Her mood symptoms and mental state showed significant improvement with this combination. But 3 weeks later she developed conjunctivitis and swelling of the lips,

followed by painful erosion in the oral mucous membrane and erosive bloody crust on her lips (Figure 1). Both her hands and legs were covered with erythematous and bullous eruptions with detachment of skin (Figure 2). Eye examination revealed significant chemosis with membrane formation on the palpebral conjunctiva bilaterally. History revealed that no such lesion occurred earlier. Family and personal history was insignificant. Vital signs were within normal limits. As the symptoms worsened, she was referred to a general medical hospital and was clinically diagnosed as a case of Stevens-Johnson syndrome. All her routine investigations were normal except high C-reactive protein. Lamotrigine was stopped immediately and necessary treatment protocol for the condition was started. Her condition improved to some extent in the next 2 weeks and patient was discharged with an antidepressant and an antipsychotic.

Figure 1: Bloody crust on the lips

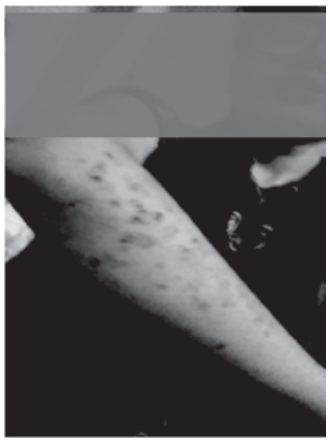

Figure 2: Erythematous lesions on hand with skin detachment.

Discussion

Stevens-Johnson syndrome is a fatal medical emergency that has been reported to be linked with 100 different types of medications. Hypersensitivity reaction can occur by any antiepileptic drug, but serious cutaneous reactions occur only in small number of patients. Lamotrigine is a novel antiepileptic, not only used as an effective treatment for partial or generalized seizure, but also has been effective for bipolar and other psychiatric disorders as well.[6] The incidence rate of lamotrigine induced SJS while treating seizure is 1% in children, 3% in adult, and in 16% cases there are history of past use of an antiepileptic drug.[6,7] When Lamotrigine is used as monotherapy, the risk of development of rash is 0.08% but 0.13% for adjuvant therapy.[6] SJS is more common in females than males and the incidence increases rapidly with an increase in age. The average age for development of SJS is between 46 and 63.[1] But Schlienger et al, after studying 53 cases of lamotrigine induced skin reaction, found that most of the patients who developed SJS were below 18 years of age and their numbers were higher than other age group.[8] In our case, patient was a 19-year old female using lamotrigine for last 3 weeks. No systemic and viral causes were detected. Rapid dose escalation as well as a single large dose of lamotrigine is directly linked to the increased risk of SJS.[6] The recommended starting dose is 25mg daily for first 2 weeks followed by 50 mg daily for next 2 weeks. Then increases of 50-100 mg as clinically indicated.[2,6] We started 50 mg in divided doses from first day of treatment then after 2 weeks we increased the dose to 100mg, which could be a causative factor for this case. SJS is a serious adverse hypersensitivity reaction that demands immediate management. As the risk of development of SJS is rare with lamotrigine, but mortality rate is high (about 5-15%),[2] so proper identification of the causative factors as well as adequate treatment can reduce the mortality rate.

Conclusions

Stevens- Johnson syndrome is a potentially life-threatening condition and the severity and adversity of the condition suggests immediate application of appropriate intervention. Prevention of lamotrigine induced SJS must be attempted from the beginning, which includes ethical prescribing, gradual addition and careful monitoring of drug combinations and excluding viral and other systemic infections, even though idiopathic factors may play a role.

Nadia Afroz, MD phase B Resident, Psychiatry, National Institute of Mental Health, (NIMH), Dhaka, Bangladesh; **Rubina Hossain,** FCPS part 2 Trainee, Psychiatry, NIMH, Dhaka, Bangladesh; **Shaafi Raaisul Mahmood,** MD Phase B Resident, Psychiatry, NIMH, Dhaka, Bangladesh; **Mohammad Tariqul Alam,** Associate Professor, Psychiatry, NIMH, Dhaka, Bangladesh.

Correspondence: Nadia Afroz, MD phase B Resident, Dept. of Psychiatry, National Institute of Mental Health, (NIMH), Dhaka, Bangladesh.
Email: chaityami@gmail.com

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