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Case Report

Lamotrigine-induced Stevens-Johnson syndrome in a 25 year old lady

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ABSTRACT

Stevens-Johnson syndrome (SJS) is an immune-complex mediated hypersensitivity reaction and has been linked as an adverse side effect to many drugs. This case is about a 25 year old woman who had lamotrigine-induced Stevens-Johnson syndrome which is known to occur but is rare. Lamotrigine, an anticonvulsive medication and also a commonly used mood stabilizer was prescribed to the patient to treat symptoms of anxiety and depression. The patient developed Stevens-Johnson syndrome 5 weeks after start of therapy. This case is discussed for its relevance to the use of lamotrigine which is currently prescribed very commonly in psychiatric practices.

Keywords: Hypersensitivity reaction, Lamotrigine, Stevens-Johnson syndrome

INTRODUCTION

Stevens-Johnson Syndrome (SJS) and toxic epidermal necrolysis (TEN) are immunecomplex-mediated hypersensitivity reactions that typically affects the skin and the mucous membranes leading to necrosis and sloughing of the epidermis. The most common etiology of SJS/TEN is hypersensitivity to certain drugs like, antibiotics, anticonvulsants and nonsteroid anti-inflammatories and allopurinol.[1]

Among anticonvulsants, SJS is rarely caused by lamotrigine, which is also used as a mood stabilizer.[2,3] Various adverse effects associated with lamotrigine include headache, dizziness, somnolence, nausea, aggressiveness, insomnia and rash.[4] The overall incidence of lamotrigine-induced serious rash is approximately 0.3 percent in adult patients with epilepsy receiving adjunctive therapy.[5] Exact rates of Stevens-Johnson syndrome with lamotrigine are not known, but are reported as 0.02 percent in adults from the German Rash Registry.[6] Though there has been a few reported cased of lamotrigine-induced SJS in Indian patients with epilepsy in combination with valproic acid, we can find no report of SJS in Indian patients of mood disorders on lamotrigine therapy without concomitant use of valproic acid.[7]

Here we report a rare case of lamotrigine-induced SJS in a 25 year old Indian patient suffering from Schizoaffective disorder. Use of the Naranjo algorithm scale indicated a probable relationship of causality with a score of 6.[8]

CASE REPORT

Patient is a 25 year old female housewife, resident of a rural area who has been suffering from schizoaffective disorder from 6 months and was prescribed haloperidol, divalproex sodium, lorazepam and metformin. After 4 months of therapy, lamotrigine 25 mg once daily was added to the regimen due to poor control of her symptoms. After about 5 weeks of lamotrigine therapy, the patient developed fever, chills, headache and rash over the whole body. She also became gradually intolerant to spicy food and developed oral lesions over a week. A week later, the patient was presented to our hospital.

On examination, erythematous maculopapular rash over her trunk and extremities were seen (Figures 1b, c and d). Bullous eruptions and detachment of epidermis on the face, haemorrhagic crusts over lips and erosion of mucous membrane inside her mouth were present (Figure 1a). Multiple genital lesions were also seen. She was admitted for further treatment and was kept under the care of a dermatologist, a gynaecologist and a psychiatrist.

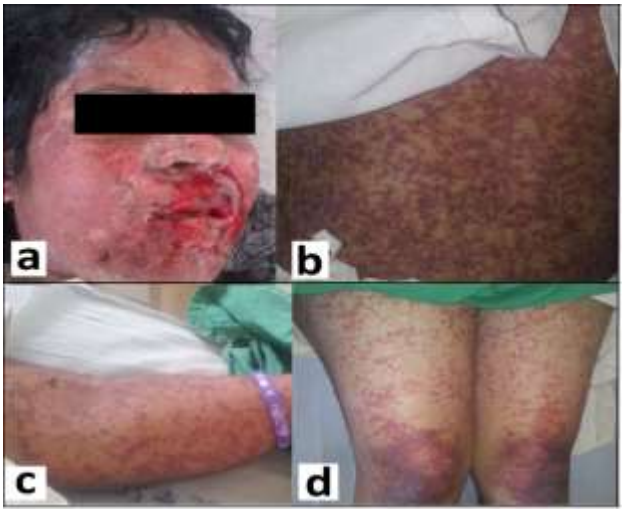

Figure 1: (a) Ulcerative lesions on lips and detachment of epidermis on the face; Erythematous maculopapular rash over (b) trunk (c) arms (d) thighs.

The extent of epidermal detachment was less than 10%. On the basis of history and clinical examination a diagnosis of Steven Johnson's syndrome due to the use of lamotrigine was made. Lamotrigine was discontinued and patient was managed symptomatically and supportive treatment was started. Patient was started on intravenous fluids, intravenous antibiotic augmentin, intravenous corticosteroids, calamine lotion, benzocaine gel and triamcinolone dental paste. Tetanus prophylaxis was given. With aggressive supportive care the dermatological condition of the patient started to improve in few days without any complications.

DISCUSSION

Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN), are severe idiosyncratic reactions with a reported incidence of around 2.6 to 6.1 cases per million people per year with a mortality rate of around 5%.[9] SJS is named after two American paediatricians, Albert Mason Stevens and Frank Chambliss Johnson, who jointly published the first description of the disorder in the American Journal of Diseases of Children in 1922.[10] SJS/TEN are immune-complex-mediated hypersensitivity reactions caused by certain drugs, infections and rarely, cancers.[11] SJS/TEN characteristically involves skin and mucous membrane with painful eruptions and epidermal detachment.

Although several classification schemes have been reported, the simplest breaks the disease down as follows.[12]

- *Stevens-Johnson syndrome (SJS):* A "minor form of TEN" with less than 10% body surface area (BSA) detachment.
- *Overlapping Stevens-Johnson syndrome/toxic epidermal necrolysis (SJS/TEN):* Detachment of 10-30% BSA.
- *Toxic epidermal necrolysis (TEN):* Detachment of more than 30% BSA.

SJS is a serious systemic disorder with the potential for severe morbidity and even death. Clinical features of SJS include involvement of skin and oral, nasal, eye, vaginal, urethral, gastrointestinal, and lower respiratory tract mucous membranes. Skin rash can begin as macules that develop into papules, vesicles, bullae, urticarial plaques or confluent erythema leading to edema, sloughing, blistering, ulceration and necrosis. Gastrointestinal and respiratory involvement may also progress to necrosis.[13]

Medications are the leading trigger of SJS in adults. In addition to medications, conditions such as malignancies, systemic lupus erythematosus and viral infections may trigger SJS. Drug etiologies include reaction to antibiotics, antiepileptics, non-steroidal anti-inflammatory drugs, anti-malarial and allopurinol.[14,15] SJS has also been associated with immunisation, e.g. measles and hepatitis B.[16]

The pathogenesis of SJS is yet to be clarified. The scenario suggested by today's literature points toward drug-specific CD8+ cytotoxic T-cells utilizing perforin/granzyme B triggered apoptosis of epithelial cells.[17] SJS has been reported from concomitant use of valproic acid and lamotrigine but reports of Lamotrigine alone causing SJS are relatively rare.[18,19]

Lamotrigine is a potential anti-epileptic drug which is also used as a mood stabilizer.[3] Side effects of Lamotrigine generally include CNS symptoms like headache, sleep disturbance, movement disorder, hallucinations,

gastrointestinal symptoms like diarrhoea, nausea, vomiting, hepatic dysfunction and skin & cutaneous side effects like rash. Stevens-Johnson syndrome has also been mentioned as a rare hypersensitivity reaction/side effect of lamotrigine.

Though our patient was concomitantly on haloperidol since four months before the addition of lamotrigine to her drug regimen, it is unlikely that Haloperidol was the cause of her SJS because symptoms of SJS were seen 5 weeks after being on lamotrigine add-on therapy. Mechanisms for lamotrigine-induced SJS are less well understood but recent evidence suggests that antiepileptic drug-related hypersensitivity may be a consequence of chemotoxic and immunologically mediated injury; however, the pathogenesis of this reaction may vary somewhat among different antiepileptic drugs.[20] We are reporting this case, since there is increasing use of lamotrigine in psychiatry (especially as a mood stabilizer) and because of the rarity of Stevens-Johnson syndrome (SJS) as an adverse effect of lamotrigine which can have very high mortality and morbidity.

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