Oxcarbazepine-induced Stevens Johnson syndrome: A rare case report

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ABSTRACT

Although carbamazepine is the most common cause of Stevens Johnson syndrome (SJS) a new antiepileptic drug, oxcarbazepine which is structurally related to carbamazepine, has also been rarely shown to induce SJS. Here we report a case with SJS, which was induced by oxcarbazepine.

Key words: Oxcarbazepine, Solitary small enhancing computerized tomography lesion, Stevens-Johnson syndrome

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INTRODUCTION

Stevens–Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN), defined by widespread blisters arising on macules and/or flat atypical targets are diseases with homogenous clinical characteristics and a potentially lethal outcome.[1] SJS is usually associated with several antiepileptic drugs including carbamazepine, lamotrigine, phenobarbital, phenytoin, and valproic acid.[2] A new antiepileptic oxcarbazepine, which is structurally related to carbamazepine (CBZ), was introduced for use in patients with epilepsy. First synthesized in 1966, it was eventually approved for use as an anticonvulsant in EU countries and India in 1999.

According to a review of the literature, it appears that oxcarbazepine-induced SJS has rarely been reported.[3] Here we report a rare case of oxcarbazepine-induced SJS.

CASE REPORT

A 21-year old male presented with two episodes of right parietal with secondary generalized epilepsy since 2 weeks. Physical examination showed unremarkable findings. CT scan of head with contrast revealed left parietal lobe solitary small enhancing computerized tomography lesion (SSECTL) with mild edema. Electroencephalography (EEG) showed normal awake recordings. He was treated with oxcarbazepine 300 mg twice a day which was gradually titrated to 600 mg twice a day within a week. The patient developed high fever and multiple maculopapular eruptions [Figures 1-3] were found over the patient's face and trunk around the 14th day of taking oxcarbazepine. Two to three days later, some blisters were also observed on his upper extremities. This way s followed b multiple oral ulcers and hyperemic conjunctivae.

He was admitted in neurology ward with the help of dermatologist with the diagnosis of SJS. Laboratory investigations showed leucocytosis (WBC, 14630/l, reference value, 4000–11 000/l) and elevated C-reactive protein 60.78 g/ml; reference range, 0–5 g/Ml.

A skin biopsy was also performed to confirm histopathology.

The stratum corneum layer appeared to be normal. There was marked liquefactive degeneration with some dyskeratotic keratinocytes. The dermis showed lymphohistiocytic infiltration around blood vessels and scanty eosinophils. The skin pathology was consistent with SJS.

DISCUSSION

The diagnosis of SJS is based on clinical manifestations with acute onset of rapidly expanding targetoid erythematous macules, necrosis and detachment of the epidermis along with erythema, erosions, and crusting of two or

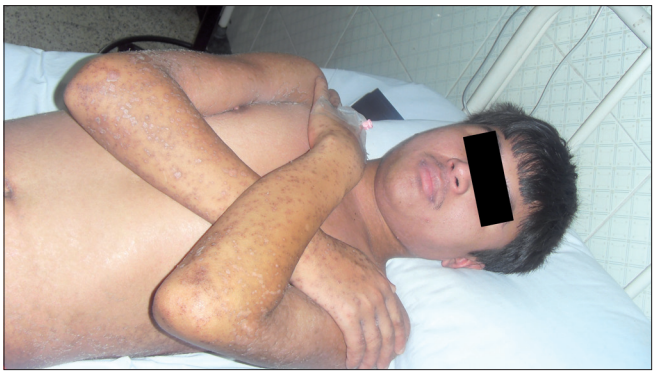

Figure 1: Targetoid rashes over both upper extremities, conjuctiva and oral mucosa in resolution after 2 weeks of treatment

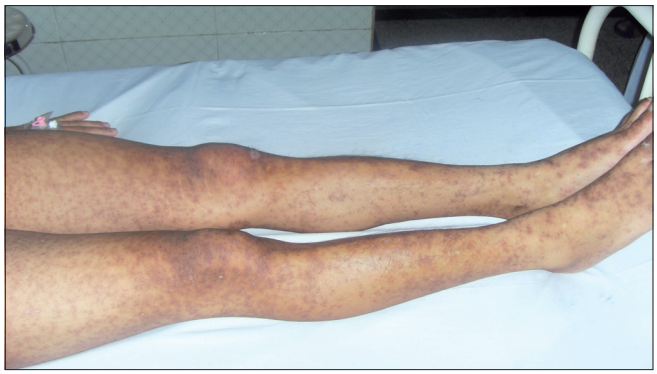

Figure 2: Targetoid rashes over both lower extrimities, 2 weeks of oxz initiation

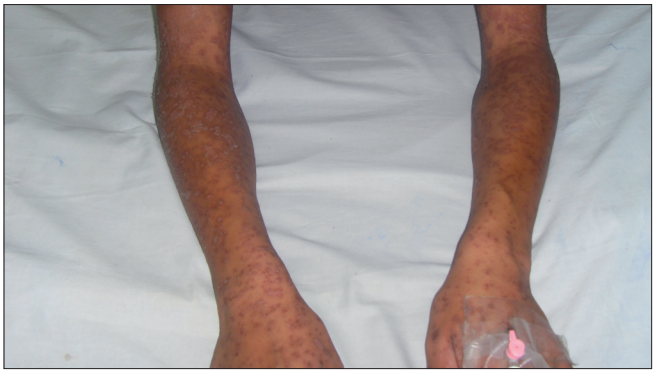

Figure 3: Targetoid rashes over upper extremities

more mucosal surfaces.[4] Oxcarbazepine, the incriminated drug in this case was first synthesized in 1966,was approved for use as an anticonvulsant in Denmark in 1990,was approved in Spain in 1993, in Portugal in 1997, and eventually for all other EU countries and in India in 1999. It was approved in the US in 2000.

The patients usually develop a hypersentivity reaction to this drug between 2 and 12 weeks after commencing treatment with it.[5] Our patient had targetoid erythematous eruptions and mucosal involvement 2 weeks after starting oxcarbazepine treatment. During these 2 weeks he took no medicine except for oxcarbazepine. The skin pathology finding revealed lymphohistiocytic infiltration around the blood vessels and scanty eosinophils, which was consistent with SJS.

In this case, we used 300 mg of oxcarbazapine twice daily for seizure control and then increased the dose to 600 mg twice daily. Both the initial and titration doses were slightly lower than the recommended doses. It has been reported that higher daily doses of drugs are associated with increased risk of SJS just as is the case for allopurinol.[6] However, there is no evidence about the relationship between oxcarbazepine dosage and SJS.

Although many factors have been proposed as risk factors of SJS including adverse drug effects, malignant disorders or graft-host disease and infections, most of them were induced by drugs. The most common drugs are anticonvulsants, particularly carbamazepine.(CBZ).[7] To our knowledge, there are no reports of oxcarbazepine-induced SJS from India. According to the Food and Drug Administration the incidence of oxcarbazepine-induced SJS is estimated to range between 0.5 and 6 cases per million people per year within general population.[8] The incidence of carbamazepine-induced SJS is higher than that for oxcarbazepine induced SJS. The reason why oxcarbazepine has fewer side effect is that oxcarbazepine is almost completely metabolized through reduction and conjugation to yield an active monohydroxy derivative. In contrast, the oxidation of CBZ to 10, 11-epoxide is regarded as the most common cause of adverse effects.[9] The pathogenesis of SJS remains unclear and there is considerable debate whether to treat SJS with systemic steroids. However, Lam *et al,* found that the early use of short-term systemic steroids for 3–5 days lacked any significant side effects and did not increase mortality or morbidity in children.[10] Our patient was treated with intravenous steroid and antihistamine for 7-9 days. His condition improved and he was discharged 14 days after admission. No sequelae were found during 2 months of follow-up.

In conclusion, we have described perhaps the first case of oxcarbazepine-induced SJS in India. We need to recruit more patients to elucidate the pathogenesis of oxcarbazepine-induced SJS.

REFERENCES

1. Auquier-Dunant A, Mockenhaupt M, Naldi L, Correia O, Schröder W, Roujeau JC, *et al*. Correlations between clinical patterns and causes of erythema multiforme majus, Stevens-Johnson syndrome, and toxic epidermal necrolysis: Results of an international prospective study. Arch Dermatol 2002;138:1019-24.
2. Mockenhaupt M, Messenheimer J, Tennis P, Schlingmann J. Risk of Stevens-Johnson syndrome and toxic epidermal necrolysis in new users of antiepileptics. Neurology 2005;64:1134-8.

3. Lin LC, Lai PC, Yang SF, Yang RC. Oxcarbazepine-induced Stevens-Johnson syndrome: A case report. Kaohsiung J Med Sci 2009;25:82-6.
4. Frisch PO, Ruiz-Maldonado R. Erythema multiforme, Stevens-Johnson syndrome and toxic epidermal necrosis. In: Freedberg IM, Eisen AZ, Wolf K, editors. Fitzpatrick's Dermatology in General Medicine. 6th ed. New York: McGraw-Hill, 2003. p. 543-57.
5. Pirmohamed M, Lin K, Chadwick D, Park BK. TNFα promoter region gene polymorphism in carbamazepine-hypersensitive patients. Neurology 2001;56:890-6.
6. Halevy S, Ghislain PD, Mockenhaupt M, Fagot JP, Bouwes Bavinck JN, Sidoroff A, *et al*. Allopurinol is the most common cause of Stevens-Johnson syndrome and toxic epidermal necrolysis in Europe and Israel. J Am Acad Dermatol 2008;58:25-32.
7. Devi K, George S, Criton S, Suja V, Sridevi PK. Carbamazepine- the commonest cause of toxic epidermal necrolysis and Stevens-Johnson syndrome: A study of 7 years. India J Dermatol Venereol Leprol 2005;71:325-8.
8. Dogan EA, Usta BE, Bilgen R, Senol Y, Aktekin B. Efficacy, tolerability, and side effects of oxcarbazepine monotherapy: A prospective study in adult and elderly patients with newly diagnosed partial epilepsy. Epilepsy Behav 2008;13:156-61.
9. Schmidt D, Elger CE. What is the evidence that oxcarbazepine and carbamazepine are distinctly different antiepileptic drugs? Epilepsy Behav 2004;5:627-35.
10. Lam NS, Yang YH, Wang LC, Lin YT, Chiang BL. Clinical characteristics of childhood erythema multiforme, Stevens - Johnson syndrome and toxic epidermal necrolysis in Taiwanese children. J Microbiol Immunol Infect 2004;37:366-70.

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