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Oxcarbazepine induced Erythematous Rash: A Case Report

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ABSTRACT

Newer anti-epileptics like oxcarbazepine are known to have better side effect profile as compared to its primary congener carbamazepine and are hence preferred as treatment alternatives in seizure control.The present report describes a case of oxcarbazepine induced erythematous rash in a 24 year old depressive female. This rash involving upper arms and neck subsided on discontinuation of oxcarbazepine, followed with symptomatic treatment of the reaction.

INTRODUCTION

Oxcarbazepine (OXC) has been approved as a monotherapy or adjunctive therapy for the management of partial and secondarily generalized seizures, owing to its similar clinical effectiveness as compared to carbamazepine in seizure control.[1] Early studies have demonstrated that the incidence of cutaneous adverse drug reactions (cADRs) induced by OXC is less than that induced by carbamazepine (CBZ), [2]making OXC a viable alternative for patients who cannot tolerate CBZ. Recently, however, it has been reported that OXC-related skin rashes are also prevalent, with an incidence of 59%, and lead to drug discontinuation in almost all patients who experienced such adverse reactions.[3]

Anti-epileptic drug induced cutaneous adverse drug reaction includes conditions ranging from erythematous rash, mild maculopapular eruption and hypersensitivity syndrome, to the more severe forms like Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN) and has been reported in up to 10% of patients on OXC therapy.[4]

The present case describes a 24 year old female developing erythematous rash on oxcarbazepine intake.

CASE REPORT

A 24 year old female diagnosed with bipolar affective disorder, presented to outpatient department with a recent history of convulsion persisting for few minutes accompanied with headache. There was no associated history of unconsciousness or aura. She was assessed on baseline for laboratory investigations which were essentially unremarkable. She was initiated on twice daily treatment with oxcarbazepine (300mg) along with once daily dosing of sertraline (50mg), moclobemide (25mg) and lorazepam (0.5mg) which were continuing previously. After 9 days of treatment initiation with oxcarbazepine, patient presented with erythematous rash all over the upper arm and neck initiating one day prior to her reporting (Figure 1). Oxcarbazepine was suspected to be the offending medication for this reaction and was thus withdrawn. The reaction was symptomatically treated with emollients and antihistaminics and was gradually resolved within 6 days. Patient was reintroduced with levetiracetam (500mg) twice daily. The patient continued uneventful thereafter.

DISCUSSION

Oxcarbazepine (OXC), a newer anti-epileptic drug is a 10-keto analog of carbamazepine, acts by blockage of voltage sensitive sodium channels resulting in stabilization of hyper-excited neural membranes, inhibition of repetitive neuronal firing and inhibition of the spread of discharges. Adverse reactions like dizziness, drowsiness, blurred or double vision, fatigue, headaches, nausea, and vomiting are reported though less frequent.

The initial reports of OXC having fewer side effects than carbamazepine, had contributed to its popularity as a first line anticonvulsant.[5]The better safety profile of OXC is due to the

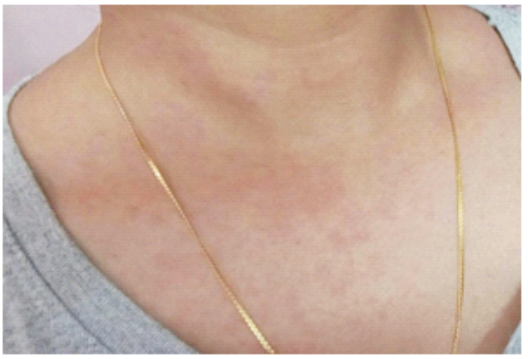

Fig. 1 : Erythematous rash involving the neck region

fact that unlike carbamazepine, it is not metabolized to an epoxide derivative. This epoxide is responsible for some of the toxic effects of carbamazepine. OXC's biotransformation is largely by hydroxylation, to an active non-toxic 10-monohydroxy metabolite (MHD: 10,11 dihydro-10-hydroxy-5H-dibenzol [b,f]azepine-5-carboxamide).

However, about 3% of patients under antiepileptic therapy develop a cutaneous adverse reaction - often morbilliform exanthem (50-95%) or urticaria (5-22%) - that appears within 3-20 days from the beginning of therapy and disappear spontaneously when the drug is discontinued. More rarely, antiepileptics cause severe cutaneous reactions with mortality rates ranging from 1-5% for Steven-Johnson syndrome to 5% for exanthematous pustulosis, 10% for DRESS syndrome and up to 25-30% for toxic epidermal necrolysis. Overall, antiepileptic drugs are the most common cause of severe cutaneous adverse reaction and, among these drugs, the risk is particularly high for phenytoin, phenobarbital, carbamazepine and oxcarbazepine (aromatic compounds).[6]The underlying mechanism of these reactions remains unclear and has been suggested to be multifactorial.Potential risk factors include age, gender, dosage, drug titration schedule, comedications and individual immunological status.[7]

In the present case, replacing OXC with levetiracetam gradually subsided the reaction accompanied with symptomatic treatment. The dechallenge test was positive but rechallenge was not done. According to Naranjo's scale[8], it appears to have a probable causal relation with a score of 5 and WHO-UMC causality assessment[9] also shows a probable/likely cause of it. Severity assessment [10]of the reaction conferred it to be of moderate grade.

CONCLUSION

Early detection and withdrawal of offending medication is the first and foremost step of managing a cutaneous adverse reaction. Opting to safer monotherapies as alternative treatment approach must go hand in hand with focused pharmacovigilance for ensuring better patient safety.

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