IJBCP International Journal of Basic & Clinical Pharmacology

DOI: http://dx.doi.org/10.18203/2319-2003.ijbcp20170350

Case Report

A rare case of oxcarbazepine induced Stevens Johnson Syndrome: toxic epidermal necrosis overlap

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Received: 12 December 2016 Accepted: 03 January 2017

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ABSTRACT

Oxcarbazepine is a closely related analogue of carbamazepine and is useful in the monotherapy of seizures with an improved toxicity profile. Its clinical safety has been recently put under scrutiny as evidence has emerged about its adverse drug reactions and it is increasingly being reported to cause cutaneous drug eruptions. Here we report a rare case of oxcarbazepine induced Stevens Johnson - toxic epidermal necrolysis overlap.

Keywords: Adverse drug reaction, Oxcarbazepine, Stevens Johnson Syndrome (SJS), Toxic Epidermal Necrolysis (TEN)

INTRODUCTION

Stevens Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are potentially lethal idiosyncratic adverse drug reactions. SJS is characterised by the appearance of erythematous or purpuric macules with irregular shape and size. Blisters often occur on all or part of the macule. The lesions are widespread but the confluence of individual lesions remains limited, involving less than 10% of the body surface area. SJS-TEN overlap is characterized by confluent blisters which result in detachment of the epidermis and erosions on 10% to 29% of the body surface area whereas in TEN

there is widespread detachment of epidermis on more than 30% of the body surface area. The commonly incriminated drugs causing SJS/TEN are anticonvulsants, sulfonamides, nonsteroidal anti-inflammatory drugs and antibiotics.² anticonvulsants, Amongst the carbamazepine, lamotrigine, phenobarbital, phenytoin and valproic acid are known to cause SJS/TEN.3 Oxcarbazepine (OXC) is a 10-keto analogue of carbamazepine and has better reported safety profile as a first line agent for epilepsy monotherapy. Reported cases of SJS/TEN due to OXC are rare. 4-7 Here we report a case of SJS due to OXC in a patient of seizures following neurocysticercosis.

CASE REPORT

An 11 year old male child presented to the emergency room of a tertiary care hospital with chief complaints of erythematous, pruritic rashes with excoriation all over the lower extremities (Figure 1), lower back and neck along with low grade fever for 2 days. The child had a history of recurrent focal seizures with loss of consciousness 2 weeks ago, for which he was hospitalised and investigated thoroughly. MRI spectroscopy had revealed a ring enhancing calcified cystic lesion in the left frontal lobe which was diagnosed as neurocysticercosis. Consequently he was put on a course of albendazole (15 mg/kg of body weight twice daily p.o.), prednisolone (15 mg once daily p.o.) and oxcarbazepine (300 mg twice daily). He was discharged after 5 days with an advice to continue oral prednisoslone (in tapering dose for 1 week), albendazole (15mg/kg twice daily for another 3 days) and oxcarbazepine (300 mg twice daily). The patient started to develop macula-papular rashes over his legs and back after one week (Fig 1, 2), but the parents failed to report this to the treating physician. According to them these rashes merged with each other gradually and blisters started to appear along with fever. Laboratory investigations showed marked leukocystosis, normal liver and renal function panels, elevated ESR and significantly elevated CRP. Skin biopsy revealed extensive necrosis of the epidermis. The dermoepidermal junction and epidermis was infiltrated with lymphocytes. The child was presumed to be suffering from SJS-TEN overlap by the attending dermatologist and OXC was immediately discontinued. This was substituted by anti epileptic drug levaricetam along with hydroxyzine and a tapering dose of dexamethasone.





Figure 1: Multiple erythematous, maculopapular rashes with excoriation present over (A.) the legs, feet and (B.) the lower back.

Calamine lotion was advised for local application and proper aseptic conditions were maintained. Albendazole was reintroduced after 4 days without any further adverse event. The child responded well to this therapy and was discharged after 11 days; the rashes gradually disappeared over 2 weeks and have been followed up by the treating physician regularly since then without further event.

Based on available clinical information this case had a Naranjo score of +8 i.e. probable adverse drug reactions (ADR).⁸ The WHO-UMC criteria for causality revealed this ADR as being probable/likely due to OXC intake.⁹ Assessment of Hartwig's severity revealed a level 3 score (as the ADR required that treatment with the suspected drug is stopped and an antidote was given to counter the ADR).¹⁰

DISCUSSION

SJS and TEN are characterised by widespread blisters arising on macules and/or flat atypical target oid rashes. diseases with homogeneous They are characteristics, a potentially lethal outcome and an probability of being drug induced.1 elevated Oxcarbazepine (OXC) is a 10-keto analogue of carbamazepine and it acts as an anticonvulsant 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. 11 Skin rash is relatively common (up to 10% of all patients) and is the main reason for discontinuation of the drug in the comparative monotherapy studies.⁵ Oxcarbazepine may cause hyponatraemia probably due to an antidiuretic hormonelike effect.¹² The initial reports of OXC having fewer "severe" side effects than carbamazepine, had contributed to its popularity as a first line anticonvulsant. 13 The better safety profile of oxcarbazepine is due to the 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 10monohydroxy metabolite (MHD: 10,11 dihydro-10hydroxy-5H-dibenzol [b, f]azepine-5-carboxamide).⁸ A recent study has shown the association of OXC induced cutaneous drug eruptions and HLA B*1502 allele in Han Chinese patients.14

Funding: No funding sources Conflict of interest: None declared Ethical approval: Not required

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Cite this article as: Maitra A, Bhattacharyya S, Mukherjee S, Era N. A rare case of oxcarbazepine induced Stevens Johnson Syndrome: toxic epidermal necrosis overlap. Int J Basic Clin Pharmacol 2017;6:466-8.