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Case Report

Pharmacology Section

Oxcarbazepine Induced Maculopapular Rash - A Case Report

ARUNAVA BISWAS[1], RITABRATA MITRA[2], SUKANTA SEN[3], AGNIK PAL[4], SANTANU KUMAR TRIPATHI[5]

ABSTRACT

Unlike carbamazepine, newer anti epileptic drug like oxcarbazepine, reports fewer side effects. In this report we describe a case of oxcarbazepine induced maculopapular rash probably happened because of a drug interaction with isoniazid, and a brief review of the existing literature is presented herewith. A 40-year-old male patient received oxcarbazepine 300mg twice daily along with other anti-tubercular drugs including isoniazid (300mg) once daily since two days. Extensive cutaneous rash with intense itching developed which subsided on discontinuation of oxcarbazepine. This case highlights the fact that there is a potential possibility of drug-drug interaction between oxcarbazepine and isoniazid and concomitant use of these two drugs should better be avoided during clinical practice.

Keywords: Isoniazid, Maculopapular rash, Oxcarbazepine

CASE REPORT

A 40-year-old man suffering from intermittent headache for past three years and history of right sided tubercular pleural effusion in childhood had a recent history of convulsion as a single episode associated with headache, earache and dribbling of saliva from the mouth. The convulsion persisted for few minutes and the patient uneventfully recovered from it. There was no associated history of unconsciousness or aura. The patient visited an ENT specialist and was diagnosed as a case of left sided chronic suppurative otitis media which was initially treated conservatively. Later on, he underwent a myringoplasty operation. Afterwards, on 20th postoperative day again a second episode of convulsion occurred, which persisted for few minutes followed by heaviness of the left side of the chest and weakness of the left side of the body. He was rushed to a local physician; Contrast Enhanced Computed Tomography (CECT) scan of brain was done which revealed a space occupying lesion (SOL) in the left inferior parietal lobe. Other investigations, namely serum electrolytes, liver function test, kidney function test, ultrasonography of whole abdomen did not reveal any abnormality. He was advised MRI scan and MR spectroscopy of brain but he could not afford. The patient was prescribed oxcarbazepine (300mg) twice daily, lorazepam (0.5mg) once daily and pantoprazole (40mg) once daily, all by mouth, as a preventive measure. Later suspecting a possible tuberculoma, the patient was also prescribed once daily treatment with isoniazid (300mg), rifamcipin (450mg), ethambutol (1000mg), pyrazinamide (1500mg) and vitamin B6 (40mg) all orally along with intramuscular injection streptomycin (750mg). On the very next day patient developed extensive maculopapular rash all over the body except face, palm and sole, associated with severe itching. The treating physician stopped oxycarbazepine immediately and prescribed oral hydroxyzine (25mg) once daily anticipating potential cutaneous adverse drug reaction. Oxcarbazepine was replaced by oral levetiracetam (500mg) twice daily for seizure control. The rash subsided completely within two days without any sequelae.

DISCUSSION

A newer anti epileptic drug (AED), oxcarbazepine is a 10-keto analog of carbamazepine. The clinical effectiveness of oxcarbazepine is similar to that of carbamazepine, but with fewer adverse drug reactions (ADRs), perhaps due to their different metabolic pathways [1]. Oxcarbazepine has side effects though less frequent, share some ADRs of carbamazepine like dizziness, drowsiness, blurred or double vision, fatigue and may cause headaches, nausea, and vomiting but unlike carbamazepine idiosyncratic cutaneous adverse drug reaction (cADRs) is very rare with oxcarbazepine.

AED induced cutaneous adverse drug reaction ranges from mild maculopapular eruption (MPE) and hypersensitivity syndrome, to the more severe Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN). Among these cADRs, MPE is most common [2], and is generally considered an initial form of the other, more severe, cADRs. There is also reporting on CBZ induced severe cutaneous reactions [3] but none with oxcarbazepine among Indian population. In the present case the possible mechanism behind such ADR might be due to drug- drug interaction. Isoniazid (INH) is an inhibitor of the CYP3A enzyme whereas oxcarbazepine is an inducer of CYP3A4/5 and also metabolized by the same enzyme as well. Simultaneous administration of these two drugs might have interfered with the metabolism of oxcarbazepine thereby increased its serum concentration to a higher level that produced such toxicity. Replacing oxcarbazepine with levetiracetam abolished such interaction and the rash subsided. The dechallenge test was positive but rechallenge was not done. According to Naranjo's scale [4] it appears to have a probable causal relation with a score of 5 and WHO-UMC [5] causality assessment also shows a probable/likely cause of it. On the other hand according to modified "Hartwig and Siegel – 1992 ADR Severity Assessment Scale" [6] it was calculated as a 'moderate level 3' type of ADR.

There are many reports of dose dependent cutaneous toxicity of carbamazepine but there are scanty such reports of drug interactions leading to oxcarbazepine induced cutaneous adverse reaction as possibly happened in this case. Two studies done earlier documented cutaneous toxicity with oxcarbazepine depicted in the [Table/Fig-1]. One of this study documented no significant association between HLA-B*1502 and OXC-MPE [2].

CONCLUSION

Oxcarbazepine may interact with INH when administered simultaneously leading to such cutaneous ADR. It is probably better to avoid the co-administration of such drugs and opt for alternative anticonvulsant treatment option keeping unchanging the treatment antitubercular drug regimen as far as practicable. Exercising caution is essential to avoid this preventable problem.

Author	Type of study	Findings
Hu FY et al., [2]	Prospective study	HLA-B*1502 allele may contribute to the genetic susceptibility to OXC-induced MPE in Chinese Han population.
He N et al., [7]	Prospective study	Incidence of OXC-induced cADRs was low, and no severe reactions occurred. No significant association between HLA-B*1502 and OXC-MPE was found.
Wang X et al., [8]	Retrospective study	8.92% of cutaneous adverse drug reaction attributed to oxcarbazepine among AEDs
Keshri U [9]	Case study	Toxic epidermal Necrolysis with leucocytosis, elevated C - reactive protein with oxcarbazepine 300mg/day
Wal P et al., [10]	Case report	Stevens–Johnson syndrome with leucocytosis, elevated C - reactive protein with oxcarbazepine 900mg/day
Sharma SR et al., [11]	Case report	Stevens–Johnson syndrome with leucocytosis, elevated C - reactive protein with oxcarbazepine 600mg/day

[Table/Fig-1]: Literature reporting oxcarbazepine induced maculopapular rash

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PARTICULARS OF CONTRIBUTORS:

1. Post Doctoral Trainee, Department of Clinical & Experimental Pharmacology, Calcutta School of Tropical Medicine, 108, C.R. Avenue, Kolkata, India.
2. Assistant Professor, Department of Pulmonary Medicine, Institute of Post Graduate Medical Education & Research, Circus Ave, Bhawanipur, Kolkata, India.
3. Post Doctoral Trainee, Department of Clinical & Experimental Pharmacology, Calcutta School of Tropical Medicine, 108, C.R. Avenue, Kolkata, India.
4. Post Graduate Trainee, Department of Clinical & Experimental Pharmacology, Calcutta School of Tropical Medicine, 108, C.R. Avenue, Kolkata, India.
5. Professor and HOD, Department of Clinical & Experimental, Pharmacology, Calcutta School of Tropical Medicine, 108, C.R. Avenue, Kolkata, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Arunava Biswas,
Ganga-505, Godrej Prakriti, 187F/1 B.T.Road, Sodepur, Kolkata-7000115, India.
Phone : 9674328329, E-mai : drabiswas@gmail.com

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