Oxcarbazepine induced toxic epidermal necrolysis - a rare case report
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ABSTRACT
Carbamazepine, is well known to cause Stevens–Johnson syndrome and toxic epidermal necrolysis (TEN). Oxcarbazepine, a 10-keto analog of carbamazepine, is an anticholinergic, anticonvulsant and mood stabilizing drug, used primarily in the treatment of epilepsy. Its efficacy is similar to carbamazepine but allergic reactions and enzyme induction is low. We describe a case of oxcarbazepine induced TEN, who presented with erythematous ulcerative maculopapular rash.

KEY WORDS: Carbamazepine, oxcarbazepine, Stevens–Johnson syndrome, toxic epidermal necrolysis

Introduction
Stevens–Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN), are severe idiosyncratic reactions characterized by fever and mucocutaneous lesions leading to necrosis and sloughing of the epidermis. The most common cause is the use of medications. Among the drugs, implicated more often are allopurinol, antibiotics, anticonvulsants, and nonsteroid anti-inflammatories.[1] Anticonvulsants are one of the main triggers, causing SJS/TEN, and among anticonvulsants carbamazepine is responsible for a maximum number of cases.[2] A newer anti-epileptic drug (AED), oxcarbazepine is a 10-keto analog of carbamazepine, used primarily in the treatment of epilepsy and also in anxiety, bipolar mood disorders, and benign motor tics. Its efficacy is similar to carbamazepine, but allergic reactions and enzyme induction is low with oxcarbazepine.[3] The reported frequency of serious carbamazepine hypersensitivity reaction is between 1/1,000 and 1/10,000 new exposures to the drug.[4] However, hypersensitivity reactions to oxcarbazepine have rarely been described. Review of the literature revealed that oxcarbazepine-induced SJS has seldom been reported.[5] We could find only a single reported case of oxcarbazepine-induced SJS in an Indian patient.[6] Here, we report a rare case of oxcarbazepine-induced SJS.

Case Report
A Sixty-year-old elderly male, a known hypertensive on tablet losartan since 5 years had a hemorrhagic stroke in January 2014. He was prescribed tablet phenytoin because of recurrent generalized seizures, following the cerebrovascular accident. Because of poor control of seizures, the patient was put on oxcarbazepine, 300 mg BD with gradual tapering of phenytoin in May 2014. After 2 weeks of starting oxcarbazepine, the patient presented with a generalized rash all over the body and high-grade fever. Rash was maculopapular and more on the back. [Figures 1 and 2] Within next 2 days, he developed blisters on his upper extremities, followed by multiple oral ulcers, and hyperemic conjunctivae. Investigation reports revealed leukocytosis, elevated G-reactive protein [Table 1]. Patient’s skin biopsy revealed full-thickness necrosis of the epidermis, confirming the diagnosis of TEN. Oxcarbazepine was immediately stopped. He was started on tapering doses of steroids, anti H1, and H2 receptor blockers. Patient improved in a week. AED levetiracetam 500 mg BD was prescribed, the patient did not have a breakthrough seizure. It took another fortnight for complete resolution of lesions.

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Discussion

SJS and TEN are severe idiosyncratic reactions characterized by fever and mucocutaneous lesions leading to necrosis and sloughing of the epidermis. Depending upon the body surface area (BSA) involved, three entities are recognized:

- SJS: A minor form of TEN, with <10% BSA involvement
- Overlapping SJS/TEN: Ten to thirty percent of the BSA
- TEN: More than 30% of the BSA involved.

Medications are the leading trigger of SJS and TEN in adults. Infections are responsible for a relatively higher percentage of cases of SJS in children. In addition to medications, conditions such as malignancies, systemic lupus erythematosus, viral infections, exposure to ultraviolet rays may trigger SJS/TEN.

Among the drugs, implicated more often are allopurinol, antibiotics, anticonvulsants, and nonsteroid anti-inflammatory agents. In drug-related cases, there is a history of drug exposure 1–3 weeks preceding the onset of symptoms. A 2007 multinational study from Europe and Israel indicated that allopurinol was the most common cause of SJS and TEN in these areas. Newer drugs that have been associated with SJS and TEN include nevirapine, lamotrigine, sertraline, pantoprazole, and tramadol. Recently, in a 7 years study, concluded that anticonvulsants were the cause implicated most in SJS, especially in the first 8 weeks of treatment, and the main drug responsible (more than 80%) was carbamazepine.

A newer AED, oxcarbazepine is a 10-keto analog of carbamazepine. Oxcarbazepine is an anticholinergic, anticonvulsant, and mood stabilizing drug, used primarily in the treatment of epilepsy and also in anxiety, bipolar mood disorders, and benign motor tics. It is a prodrug which is activated to eslicarbazepine in the liver. First synthesized in 1966, it was eventually approved for use as an anticonvulsant in EU countries and India in 1999. The incidence of adverse effects reported with oxcarbazepine ranged from 46% to 68%.

The most common being drowsiness, fatigue, and dizziness. Other effects with lower incidence include headache, diplopia, ataxia, nystagmus, nausea, vomiting, epigastric discomfort, and diarrhea. Elderly patients and those on high daily doses of oxcarbazepine (25–30 mg/day) may suffer from hyponatremia (in 23% cases). Oxcarbazepine increases plasma concentrations of phenytoin and valproic acid by 20–30%. One to three days before the appearance of cutaneous lesions patient develops of fever, myalgia, and general weakness. The skin lesions are symmetrically distributed on the face and upper trunk areas. The rash spreads rapidly. The initial skin lesions are usually poorly defined macules with darker purpuric centers that coalesce. Diagnosis is clinical. However, skin biopsy helps to confirm the diagnosis, usually excluding bullous diseases not related to drug therapy. The earliest histologic finding in SJS is a perivascular mononuclear inflammatory infiltrate comprised primarily of T-lymphocytes which later clustered around dying basal keratinocytes. As the lesions progress, frank subepidermal vesiculation develops, with full thickness epidermal necrosis.

According to the World Health Organization system of causality definitions, the adverse drug reaction in this reported case is categorized as probable with Naranjo algorithm score of seven. Rechallenge was not carried out due to the inherent risk involved, and the patient showed improvement after stopping the drug. This case report documents a severe adverse reaction with oxcarbazepine which is a new AED and probably a less reported case of oxcarbazepine-induced SJS in India.
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Conflicts of Interest
There are no conflicts of interest.

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