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CASE REPORT
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Oxcarbazepine-induced Toxic Epidermal Necrolysis: A Rare Case Report

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Abstract

Anti-epileptic medications are highly susceptible to be the causative agents for Steven Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN). Even though carbamazepine (CBZ), lamotrigine are the more commonly related anti-epileptic drugs. Oxcarbazepine (OXC), a monohydrated derivative of CBZ, is considered much safer because of the various metabolic processes of the two drugs. SJS/TEN, an acute life-threatening severe mucocutaneous reaction, is characterized by widespread necrosis and detachment of the epidermis from the skin. Five to six cases per million people per year is the overall prevalence of oxcarbazepine induced SJS & TEN globally. A case of TEN induced by oxcarbazepine who recovered following early diagnosis and treatment has been reported.

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Introduction

Adverse drug reactions (ADR) are cause for about 6% of the total hospital admissions that are putting a financial strain on the healthcare system and leading to medication recalls and deaths. Cutaneous drug reactions are the most common type of adverse drug reactions. "The percentage of potentially serious reactions is around 2%."[1] Being idiosyncratic life-threatening mucocutaneous reactions, SJS and TEN are indicated by fever, necrosis, and detachment of the epidermis.

The risk is generally present during the first 8 weeks of treatment. Various studies have shown phenytoin, carbamazepine, and lamotrigine to be the most common anticonvulsants causing SJS-TEN.[2]

OXC, a 10-keto derivative of CBZ, is thought to be safer due to its distinct metabolism.[3] Oxcarbazepine is metabolized to its active metabolite, monohydroxy derivative (MHD) in contrast to carbamazepine which is readily metabolized to an epoxide metabolite. OXC has been suggested as a safer and well-tolerated alternative because of the difference in metabolism between OXC and CBZ. According to a review of data from randomized controlled trials, open studies, and retrospective chart reviews, it is beneficial in the treatment of bipolar illness in adults; however, it has not yet been approved by the FDA.[4]

OXC-induced TEN is a rare occurrence as per a review of literature.[5] "The incidence of oxcarbazepine-induced SJS/TEN in the general population is estimated to be between 5 and 6 cases per million individuals per year."[6]

We present an interesting report of a 21-year-old girl who exhibited TEN while on oxcarbazepine.

Case report

Following a relationship issue a 21-year-old female, was consulted from the Dermatology department of a tertiary care hospital with issues of low mood, lack of interest, easy fatigability, decreased sleep and appetite for a month. She was on Tab Oxcarbazepine 600 mg/day and Tab Clonazepam 0.25 mg prescribed by a private psychiatrist 12 days ago. Small red painful rashes were developed by the patient over the chest and back on the 9th day following the treatment as reported by the family members. These skin lesions progressed rapidly to involve her extremities, face, eyes and lips on the next day. There was associated pain, difficulty in swallowing and difficulty performing daily living activities.

On examination, the patient had widely spread erythematous, purpuric as well as vesiculobullous lesions, including the skin, oral cavity, mucosal membrane and genitals Fig-1). A positive Pseudo Nikolsky sign was seen. Skin detachment affected more than 10 % of the body's surface area. The patient was admitted to the dermatology department for further management with referrals to medicine and psychiatry.

Mother reported past history of one depressive episode and one hypomanic episode each lasting for a month. There was a decreased psychomotor activity and speech on mental status examination of the patient. Her affect was depressed. She had suicidal ideations and ideas of helplessness. Hamilton Depression Rating Scale (HAM-D) showed a score of 16 and a diagnosis of bipolar affective disorder–current episode of moderate depression without somatic syndrome was done (F31.30).

Investigations revealed low hemoglobin levels of 9.8 mg/dl and lymphopenia 8.6%. CRP was elevated and blood culture revealed no growth. A diagnosis of TEN was made after a thorough history and clinical examination.

The patient was started on IV Dexamethasone and Tab Hydroxyzine after stopping Tab OXC. The patient gradually improved during her hospital stay, and the lesions began to heal. Over the course of seven days, the parenteral steroid was gradually tapered and stopped. She was given Tab Escitalopram 10 mg and Tab of Clonazepam 0.25 mg in view of depressive symptoms. At the time of discharge, 50% improvement in her depressive symptoms was seen with a score of 9 as per the HAMD Scale.

Discussion

Within the first 2 months of anti-epileptic drug use, more than 90% of TEN occurs. There is a significant risk of TEN, by drugs such as CBZ and phenytoin and these responses are dose-independent and idiosyncratic.[7] After 9 days of drug administration, our patient developed rashes .

It is of utmost importance to recognise and discontinue the offending drug. The most important thing is providing supportive care with fluids, electrolytes, and temperature monitoring.

In adults and children aged 4 to 16, OXC is FDA-approved for partial seizures. By binding to sodium channels, it acts and impedes high-frequency repetitive neuronal firing. Although it is a 10-keto analogue of carbamazepine there are significant differences between the two drugs. OXC is almost completely metabolized to its keto form to give the active monohydroxy derivative (MHD), the major pharmacologically active component. Uridine 5'-diphosphate-glucuronosyltransferase is used for the glucuronidation of the hydroxyl group of MHD, and the cytochrome P-450 system has no effect on any of the enzyme pathways involved in OXC metabolism. Most of the adverse effects of carbamazepine are known to be caused by the 10, 11-epoxide derivatives of carbamazepine oxidation. "Because of this difference in the metabolism of OXC from CBZ, OXC has been proposed to be safer and well tolerated than CBZ, thus, there is no need for dose adjustments of OXC in hepatic diseases."[7]

"Recent studies have also demonstrated that cytotoxic T cells are drug-specific and directed against the native form of the drug rather than against a reactive metabolite. Both drugs share the same molecular structure of the diben-

zoazepine ring, so we speculate that this might explain why OXC can induce TEN such as CBZ."[8]

Educating the patient about recognizing the initial skin manifestations that may develop in case of severe drug reaction and appropriate drug dosing schedule is of utmost significance in the early identification of TEN. Our case report draws attention to the need for further studies in this field, which can lead to the development of safer drugs and better treatment regimens.

Conclusion

OXC is an attractive alternative to other treatment options as it has demonstrated few drug–drug interactions, its safety and tolerability profile. Herein we present an unusual instance of TEN caused by OXC. Clinicians must be aware of this adverse side effect due to the high mortality and morbidity rates of TEN. Patients should be fully informed before commencing any anti-epileptic drug, including the newer ones, and encouraged to get in touch with their treating doctor immediately if they experience any adverse cutaneous drug reaction. By careful titration of the drug and early recognition of the side effects, one can prevent life-threatening conditions such as TEN and other side effects related to the drugs.

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Conflicts of interest

There are no conflicts of interest.

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