

## Case Report

# Stevens-Johnson Syndrome Associated with Carbamazepine Use

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## Keywords

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## Abstract

Stevens - Johnson syndrome (SJS) is a serious form of adverse cutaneous drug reaction. It's commonly associated with anticonvulsant drugs. We report two cases of SJS secondary to carbamazepine (CBZ). The clinical manifestation was similar: a maculopapular eruption and vesicles with fever. Their medical history was positive for the use of CBZ. Eosinophilia was observed in the first case. Assessment of causality using the Naranjo algorithm established a probable relationship with CBZ. The diagnosis of SJS was made and CBZ was immediately discontinued with progressive improvement. Thus highlights the importance of an early diagnosis of this cutaneous drug reaction to adjust therapy and avoid complications.

## ABBREVIATIONS

CBZ: Carbamazepine; SJS: Stevens - Johnson Syndrome; EBV: Epstein-Barr virus; CMV: Cytomegalovirus

## INTRODUCTION

Stevens - Johnson syndrome (SJS) is a serious and unexpected form of adverse cutaneous drug reaction. It's commonly associated with aromatic anticonvulsant drugs [1-3]. Carbamazepine (CBZ) is, one of these drugs, frequently involved in cutaneous drug reaction. CBZ is widely used to treat partial and tonic-clonic seizures, trigeminal neuralgia and bipolar disorders.

CBZ-induced adverse reactions have been reported in as many as 30-50% including cutaneous, hematologic, renal, and hepatic disorders [4,5] of patients treated with this drug. The relative risk for CBZ of developing severe forms of cutaneous drug reaction such as SJS/ TEN is about 11% of CBZ-treated patients and fatal issue in 3-5% of them [1]. It is quite difficult to prevent SJS because drug adverse reactions occur in an unpredictable manner but early diagnosis can change the course of this disease.

## CASE REPORT

## Case 1

A 70 year-old man who had been diagnosed as having peripheral neuropathy without any other medical history. He had received carbamazepine 200 mg/day for 3 years without any discomfort. He presented to the emergency room for generalized rash with fever of 5 days duration. Initial physical exam noted a generalized maculopapular rash on the face, trunk, back and

limbs (Fig1) associated to oral ulcers. His physical examination showed: hypotension: 75/50 mmHg, tachycardia: 120 beat per minutes and fever: 38.4 °C. He received vascular filling and admitted in to our intensive care unit. 24 hours later, the skin lesions were confluent, violet with multiple bullous (Figure 2).

His laboratory tests showed leukocytosis: 12.300 e/ml with a high rate of eosinophilia: 1000e/ml, positive C-reactive protein: 78 mg/l, renal and hepatic functions were normal. Serologic tests for acute infection (IgM) by herpes viruses, Epstein-Barr virus (EBV), and cytomegalovirus (CMV) were negative. A SJS associated to CBZ was recognized and CBZ was discontinued. Skin lesions were progressively improved. Eosinophils were



Figure 1 Generalized maculopapular rash.



Figure 2 Confluent violet macular rash with multiple bullous lesions.

normalized 7 days after the initial presentation. He was discharged 14 days after admission. The cutaneous biopsy showed polymorphic lesions able to frame with hypersensitivity reactions and detachment of the epidermis indicating that our patient had presented a SJS.

## Case 2

A 56 year-old-woman was diagnosed recently with right trigeminal neuralgia, and treated by CBZ (200mg/day). At the seventh day of treatment, she developed confluent macular rash with erythema and vesicles on the face, neck, trunk, back, lower limbs and abdomen (Figure 3). She only took CBZ 200 mg daily without any other concomitant drugs. Her body temperature was 38.5°C. Her C Reactive Protein concentration was 80 mg/l and white cell count was 14900 e/ml without eosinophilia. There was not any acute renal or hepatic failure noted. The diagnosis of SJS associated with CBZ was made. CBS was discontinued and the rash was progressively improved. She was discharged 5 days after admission.

## DISCUSSION

The diagnosis of SJS is clinical; however the relationship between the causative drug and the skin reaction is not clearly established in all cases. There is no reliable laboratory test to determine the culprit drug specially if polypharmacy. According to the Naranjo algorithm [6], our patients had a probable reaction to CBZ with score 7 and 5 respectively. The case 1 had hyper-eosinophilia. No organ involvement was observed in both cases. The risk of SJS can be associated with various drugs: sulfamethoxazole-trimethoprim, lamotrigine, carbamazepine, phenytoin, phenobarbital, allopurinol, nevirapine, oxicam nonsteroidal anti-inflammatory drugs, nevirapine and lamotrigine [7].

Its etiology is still unknown. Some pathologic mechanisms of SJS have been established including the accumulation of CD8 + T lymphocytes and macrophages which induce a cytotoxic cellular immune reaction and apoptosis in the epidermis and result in the clinical presentation of SJS [7-9]. A genetic predisposition to develop drug reactions is described with carbamazepine: some researchers have emphasized the relationship between HLA-B \*1502 and SJS [10-12].

The EuroSCAR study, suggest an interval of 4 to 28 days between the initiation of treatment and first signs of SJS [7]. In

this study a variety of drugs was reported to be associated with SJS: namely anti-infective sulfonamides, anti-epileptic drugs, oxicam and non-steroidal anti-inflammatory drug, allopurinol, sertraline and others. The latency time in other reports was shorter especially with antibiotics. Some cases of SJS with chronic intake were described [9].

Clinical and hematologic abnormalities were resolved after drug withdrawal and supportive care in several weeks in our patients without sequelae. Ordonez report, in a Spanish series of 84 cases of SJS related to 9 antiepileptic drugs, a recovery period of 2 weeks [13]. Numerous studies reported a mortality rate of SJS between 1and 5% [1,7].

## CONCLUSION

CBZ is commonly involved in cutaneous adverse reactions which can be severe such Stevens-Johnson syndrome and toxic epidermal necrolysis. Early diagnosis can change the course of disease.

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Figure 3 Diffuse macular rash and erythema.

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