

# A Case Study of Oxcarbazepine-Induced Stevens-Johnson Syndrome

## Abstract

**Background:** Stevens–Johnson syndrome is a rare potentially fatal disorder characterized by mucosal membrane erosions, bullous skin lesions and epidermal detachment.

**Objective:** This case report discusses a case of a patient who developed seizures and macular rashes as a result of Stevens–Johnson syndrome induced by oxcarbazepine.

**Case presentation:** An eight-year-old girl was admitted to hospital with complaints of seizure episodes that occurred during sleep, characterized by drooling, jerky stiff upper limbs, throat sounds, and blue lips. Patient was born with severe intrauterine growth retardation and microcephaly and was diagnosed with congenital cytomegalovirus (CMV). EEG results confirmed that focal epilepsy was the underlying cause of seizures. The patient was given oxcarbazepine as an anticonvulsant medication after confirming epilepsy diagnosis. However, after two weeks of treatment, patient developed rashes and skin lesions all over her body except hands. These skin lesions and rashes were red and tan in color, swollen, itchy, scaly, dry, popular, macular and patchy. The skin detachment was less than 10% of BSA (body surface area). The Naranjo algorithm was used to check the probability of a drug reaction and through the WHO-UMC criteria for causality, it was decided that oxcarbazepine induced the syndrome. Hence, patient was diagnosed as a case of Stevens-Johnson syndrome.

## **Conclusion**

Stevens–Johnson syndrome is a rare condition that can cause rashes and epidermal detachment. It can be caused by adverse effects of medications; however, exact pathogenesis is unknown. Therefore, studies on large number of patients are required to understand the pathogenesis of oxcarbazepine-induced SJS.

Keywords: Oxcarbazepine, seizures, Stevens-Johnson syndrome, congenital Cytomegalovirus

## **INTRODUCTION**

Stevens-Johnson syndrome is a fatal and rare skin disorder with prominent manifestation in the form of skin loss, blistering, and multi-organ damage. It is a type of autoimmune disorder, which usually invades skin, mucous membranes, and can potentially cause damage to the eyes. In its symptoms, it is very much like epidermal necrolysis but is distinct from erythema multiforme. It is considered a rare complication after medication and affects one to two persons per million yearly. Eye complications occur in almost 80% of hospitalized patients and chronic ocular changes are present in about 35%<sup>(1, 2)</sup>.

Frank Chambliss and Albert Mason Stevens first described this syndrome in 1922<sup>(3)</sup>. It is distinct from toxic epidermal necrolysis and less severe. In SJS, less than 10% of bodily surface is been affected, while in toxic epidermal necrolysis it can be more than 30%. If more complications do not occur, then the lesions heal in 1-2 weeks and the patient recovers without any long-term issues. However, a severe form of skin sloughing, and secondary bacterial infections can lead to a less positive prognosis for the disease.<sup>(4)</sup>

The syndrome is diagnosed based on the character of the affected skin. Clear signs of SJS include more than 10% affected skin in first 48 hours of symptoms, specifically iris lesions with a diameter of less than 3cm, involvement of at least two mucous membranes, a positive biopsy specimen, and fever. It is seen that there are also rises in the concentrations of several human leucocyte antigen markers, including HLA-B12, HLA-B44, HLA-Aw33, and HLA-DRw53<sup>(5)</sup>. It is critical to diagnose and treat SJS quickly because it is potentially lethal. However, our patient responded well to treatment, since SJS can be also fatal. The following case report describes a patient who developed seizures and rashes as a result of Stevens–Johnson syndrome induced by oxcarbazepine.

### **EXAMINATION/CASE PRESENTATION**

An eight-year-old girl was admitted to hospital with complaints of a seizure episode in October 2021 that occurred during sleep, characterized by drooling, jerky stiff upper limbs, throat sounds, and blue lips. Patient suffered a series of three seizures from October 2021 to December 2021. The last seizure episode was on December 9, 2021. All seizures lasted for less than five minutes and patient received rectal diazepam to abort seizures. Episodes of seizures made the girl stay at home and was dependent on caregivers for feeding.

#### **Patient History:**

The eight-year-old girl was born with severe intrauterine growth retardation and microcephaly and was been diagnosed with congenital CMV. A brain MRI showed patchy delayed myelination of the deep white matter on both brain hemispheres, with evidence of cortical atrophy. The patient used a wheelchair and was fully dependent on her caregivers to support her for life activities. The patient had significant developmental milestone delay with mental retardation, hence the child was been considered in the category of People of Determination.

Patient had following problem: Congenital CMV infection, delayed neuronal myelination with brain atrophy, global developmental delay, including gross and fine motor skills, speech delay, mental retardation, hypotonia. The patient was wheelchair dependent.

**Initial Examination and Medication:**

Electroencephalography was been performed to determine any underling reasons for seizures. Recordings were been taken at 50-minute intervals. Patient was partly drowsy and then brief periods of sleep were been observed, as well as:

- Unremarkable photic stimulation
- No focal slowing or voltage asymmetry
- Short strains of rhythmic spikes were recorded in the left temporal occipital without any clinical change
- Posterior dominant rhythm was recorded as 8-9 Hertz during wakefulness
- While in the central temporal parietal region, discharges of synchronous spike waves, bilateral in nature, were been during wakefulness.

Risk factor	0	1
Age	< 40 years	> 40 years
Associated malignancy	no	yes
Heart rate (beats/min)	<120	>120
Serum BUN (mg/dL)	<28	>28
Detached or compromised body surface	<10%	>10%
Serum bicarbonate (mEq/L)	>20	<20
Serum glucose (mg/dL)	<252	>252

The Toxic Epidermal Necrolysis-specific severity of illness score (SCORTEN) is used to predict the mortality of patient suffering from Stevens-Johnson syndrome. Only three risk factors including age, no associated malignancy and less than 10% detached skin was observed in our case, indicating a positive recovery.

EEG findings supported the diagnosis of epilepsy.

For seizures, anticonvulsant oxcarbazepine was recommended with next doses with follow up plan for 2-3 months.

- Week 1: 60 mg BID
- Week 2: 120 mg BID
- Week 3: 180 mg BID
- Week 4: 240 mg BID
- Buccal Midazolam 7.5 mg x PRN for seizure > 5 min

Although medication showed positive results for preventing seizures, it resulted in severe kind of rash after two weeks of prescribing.

**Diagnosis and Treatment:**

Patient developed rash over arms and legs. Later, the rash spread to the mouth, and ulceration led to admission to the hospital. The patient had rashes all over the body except hands, which were red and tan in color, swollen, itchy, scaly, dry, papular, macular and patchy. The severity of symptoms was been rated at a seven out of ten on the pain scale. The rash lasted for six days and occurred after an infectious exposure. It was exacerbated by scratching. Two medications were effective in relieving symptoms: calamine lotion and chlorpheniramine. An integumentary examination gave following information:

Rash	Macular, papular
Shape	Symmetric
Characteristic	Blanching, indurated, raised
Margin	Discrete
Color	Red, tan

As per case reports <sup>(5, 6)</sup> the abovementioned symptoms clearly indicate the presence of Stevens Johnsons syndrome.



Figure 1: Photo of eight years old girl with crusted red lips and mouth ulceration.



Fig 2: Red rashes on foot skin



Fig 3: Scaly, dry, patchy, and macular rash on arm skin.

The Naranjo algorithm was used to check the probability of drug reaction. Naranjo algorithm is a technique to determine whether there is a causal association between a drug and identified adverse clinical event with the help of a simple questionnaire to assign probability scores <sup>(6)</sup>. Additionally, through the WHO-UMC criteria for causality it was determined that oxcarbazepine induced the syndrome. Then medication plan was changed to topiramate as follows:

Week 1: 25 mg BID

Week 2: 50 mg BID

Week 3: 75 mg BID

For symptomatic treatment: Calamine lotion/ Chlorphenamine 2 mg twice a day was been recommended. It had relieving effects and the rash disappeared after a week.

## DISCUSSION

Stevens-Johnson syndrome is been typically viewed as medical emergency induced by certain drugs, although microorganisms such as *M. pneumoniae* can be the basis of atypical cases of SJS.<sup>(7)</sup>

Malaise and a prodromal fever are initials signs of Stevens-Johnson syndrome, and were been followed by progression of mucosal and cutaneous lesions. Urogenital and ocular lesions are also prevalent. In pure SJS cases, the affected bodily surface area is less than 10%. Patients recover easily but certain skin infections can occur due to absence of intact skin barriers that may lead to complications or even death.<sup>(8)</sup>

The onset of SJS is unpredictable and it may occur in anyone on medication, regardless of age and race. However, the incidence rate of SJS is high among females. Additionally, a study published in Southern African Journal of HIV Medicine suggested that a strong link exists between human immunodeficiency virus and SJS<sup>(9)</sup>. Common causes of SJS are drug reactions to penicillin, salicylate, sulfonamides, isoniazid, phenytoin, or barbiturates. Infections such as Adenovirus, Streptococcus, Mycoplasma, and HSV can also be potential causes. About 200 drugs have been found to be associated with the onset of Stevens-Johnson syndrome. Genetic factors in some cases also play a role. Some races have HLA associations with allopurinol and anticonvulsants, while polymorphism has also been detected in some genes. Despite diverse causes, 50-60% of cases are due to drug toxicity. The most common drug, which causes SJS are sulfonamides.<sup>(10)</sup>

Clinical manifestations of the syndrome overlap with many other disorders that affect the mucous membranes and skin, such as toxic epidermal necrolysis, major and minor erythema

multiforme<sup>(11, 12)</sup>, while staphylococcal scalded skin syndrome and other drug hypersensitivity reactions also cause other differential diagnosis with SJS.<sup>(13, 14)</sup>

So, in differential diagnosis, different problems were suggested, but a keen examination of lesions and rashes proved that SJS as skin detachment was less than 10% of BSA and purpuric macules were present in patient. It was not a case of overlapping SJS/TEN and TEN because the detachment area was between 10-30% in overlap SJS/TEN and more than 30% in TEN.

Although no biopsy was done, a comparison of all symptoms and the nature of the lesions with other case studies of Stevens-Johnson syndrome confirmed our diagnosis, as confirmed by other case studies.<sup>(5, 6)</sup>

A SJS case in a patient with a history of taking SJS-inducing drugs in the eight weeks before the onset of symptoms is been classified as secondary to drug-induced SJS. On the other hand, it is considered infectious if onset of symptoms is one week before the rash appears and serology results are positive.<sup>(15)</sup> In this case, SJS was drug-induced as patient was on oxcarbazepine medication. In literature, several research and case studies point towards rare cases of the involvement of oxcarbazepine in development of SJS. Oxcarbazepine is structurally similar to carbamazepine, the most common Stevens-Johnson Syndrome-inducing anticonvulsant drug.<sup>(16,17)</sup>

## CONCLUSION

Stevens-Johnsons syndrome is a rare autoimmune disorder that affects one to two people per million annually in the United States. Reactions to drugs are responsible for 40-60% of SJS cases. Genetic factors can also play a role.

The current mainstay of treatment in SJS is the use of anti-seizure drugs such as topiramate to prevent seizures and Chlorphenamine 2 mg for symptomatic treatment.

#### **COMPETING INTERESTS DISCLAIMER:**

Authors have declared that no competing interests exist. The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

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UNDER PEER REVIEW