

**Carbamazepine induced Stevens Johnson Syndrome: a case report from a tertiary care hospital****Jyoti B. Gadhade, Rajesh S. Hiray\*, Balasaheb B. Ghongane**

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**ABSTRACT**

Stevens Johnson Syndrome is a rare but life-threatening skin disease and Carbamazepine is considered as one of the most common cause. The reported frequency of serious Carbamazepine hypersensitivity reaction is between 1/1000 and 1/10000 new exposures to the drug. Here, we report a case of a 40 year old female patient, who developed multiple ulcerative lesions all over the body three days after starting treatment with Carbamazepine for Trigeminal Neuralgia. (Worldwide Unique Number- 2017-58502 and AMC Report Number- BJGMC-Pune/Nov-2017/BBG-1860) Stevens Johnson Syndrome was diagnosed. Carbamazepine was withdrawn, and the patient was treated with topical and intravenous antibiotics. A biopsy was done which confirmed the diagnosis of Stevens Johnson Syndrome.

**Keywords:** Adverse drug reaction, Carbamazepine, Stevens Johnson Syndrome

**INTRODUCTION**

Stevens Johnson Syndrome (SJS) is characterised by blisters arising in macules or flat atypical target shaped lesions and that has a potentially lethal outcome.<sup>1</sup> The most common cause is the use of medications. Among the drugs, most commonly involved are anti-epileptics, allopurinol, antibiotics and non-steroidal anti-inflammatory drugs.<sup>2</sup> Anti-epileptics are one of the main triggers, causing Stevens Johnson Syndrome, among which Carbamazepine is responsible for maximum number of cases.<sup>3</sup>

Cutaneous drug reactions are most-common type of adverse drug reactions.<sup>4</sup> They form 2-3% of hospitalized patients. The percentage of potentially serious reactions is around 2%.<sup>5</sup> Clinically, Stevens Johnson Syndrome

presents as erythema, necrosis and extensive sloughing of the epidermis, mucosal involvement and appearance of systemic symptoms. The pathogenesis of this syndrome has not yet been established. The death of keratinocytes due to apoptosis is believed to play a key role in the mechanism.<sup>6</sup> It is very difficult to diagnose Stevens Johnson Syndrome because drug hypersensitivity reactions occur in a very unpredictable way. The incidence of SJS/TEN has been reported to be 1.5-1.8/per million persons per year.<sup>7</sup>

Carbamazepine, an iminostilbene is widely used to treat seizure disorder, bipolar disorder, trigeminal neuralgia and chronic pain and is the most common cause of drug hypersensitivity reactions.<sup>7</sup> The reported frequency of

serious Carbamazepine hypersensitivity reaction is between 1/1000 and 1/10000 new exposures to the drug.<sup>8</sup>

Here, we report a case of Stevens Johnson Syndrome secondary to Carbamazepine in a patient with trigeminal neuralgia.

### CASE REPORT

A 40 year old female, presented with sharp, intermittent unilateral facial pain over the right mandibular area and tingling sensation over the right jaw in August 2017. She was prescribed Tablet Carbamazepine 100mg daily by a private practitioner from Nanded. Post single dose, the patient developed swelling over both the lips. The patient was further advised to continue the medication. On her 4<sup>th</sup> day of medication, the patient developed rashes over the body and fluid filled lesions. The patient was then referred to Hyderabad for further management where she was taken to the casualty and admitted. There were multiple, discrete ulcers of variable size with foul smelling discharge on trunk, bilateral extremities, buttocks along with the involvement of mouth (Figures 1, 2, 3).



**Figure 1: Abscess of the lower jaw with destruction of the lips in a patient with Carbamazepine induced Stevens Johnson Syndrome.**

The total body surface area involved was 23%. On clinical examination, patient showed involvement of both epidermis and dermis. There was involvement of conjunctival mucosa, too. Lower lip showed destruction. This soon developed into abscess of the lower jaw (Figure 4). The patient was unable to swallow food and so was put on Ryle's Tube feeding. Rest of the medical history was not significant.

Carbamazepine was immediately stopped, and the patient was started on intravenous antibiotic which was a combination of piperacillin and tazobactam; fucidic acid cream 2% and calamine lotion. She was also prescribed oral potassium permanganate (KMnO<sub>4</sub>) (1:10000) and 3%

hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>) gargles with candid mouth wash. The abscess of the lower jaw was debrided under local anaesthesia. Daily dressing was done for a month. During the course of treatment, patient went into septic shock for which she was shifted to intensive care unit and was started on intravenous imipenem, colistin and oral variconazole. After two weeks, she recovered and was shifted back to ward.



**Figure 2: Ulcerative lesions over the leg in a patient with Carbamazepine induced Stevens Johnson syndrome.**



**Figure 3: Ulcerative lesions over the buttocks in a patient with Carbamazepine induced Stevens Johnson Syndrome.**

**Table 1: Laboratory investigations (as on 18<sup>th</sup> September 2017).**

Test name	Result	Reference range
<b>Complete blood count</b>		
Haemoglobin(g/dl)	8.6	12-15
White Blood Count (per cumm)	2710	4500-11,000
Differential Leucocyte Count		
Neutrophils	50%	40-80%
Lymphocytes	44%	20-40%
Monocytes	06%	2-10%
Eosinophils	0%	1-6%
Basophils	0%	<1-2%
Platelet Count (lacs per cumm)	3.14	1.5-4.5
<b>Liver function tests</b>		
Total bilirubin (mg/dl)	2.0	0.2-1.2
Serum albumin (g/dl)	1.6	3.5-5.5
Serum globulin(g/dl)		
Serum glutamic oxaloacetic transaminase(SGOT) (IU/L)	2.8	2-3.5
Serum glutamic pyruvic Transaminase (SGPT) (IU/L)	133	5-40
Serum alkaline phosphatase (IU/L)	281	7-56
Serum alkaline phosphatase (IU/L)	297	40-140
Total protein (g/dl)	4.4	6-8
<b>Renal function tests</b>		
Serum creatinine (g/dl)	2.4	0.5-1.5
Blood Urea Nitrogen (g/dl)	108	7-20
Urine-routine and microscopy	Normal	
<b>Electrolyte levels</b>		
Serum Sodium (mEq/L)	131	135-145
Serum Potassium (mEq/L)	5.5	3.5-5
Serum Chloride (mEq/L)	102	96-106
<b>C-Reactive Protein (mg/dl)</b>	96	0-3
<b>Human immunodeficiency virus (HIV)</b>	Negative	
<b>Hepatitis B surface antigen (HBsAg)</b>	Negative	
<b>Anti Hepatitis C virus</b>	Negative	

Due to financial constraints, the patient was referred to Sassoon General Hospital, Pune for further treatment and work-up where she was put on intravenous ceftriaxone (1gm twice daily), intravenous metronidazole (500mg thrice daily), amikacin (0.5g twice daily) and ondansetron (4mg twice daily). The patient was then discharged after three days. Though the neuralgia was completely treated, she was advised follow up after a month and a half for plastic surgery opinion.

Laboratory Investigations revealed anaemia, leukopenia, elevated c-reactive protein levels and altered hepatic

function tests and blood urea nitrogen levels (Table 1). Patient's skin biopsy and immunofluorescence report was consistent with Stevens Johnson Syndrome.



**Figure 4: Ulcerative lesions over the back in a patient with Carbamazepine induced Stevens Johnson Syndrome.**

## DISCUSSION

Trigeminal neuralgia is characterised by severe excruciating stabbing pain triggered by nociceptive stimuli in the distribution of one or more divisions of trigeminal nerve. The primary drug given for its treatment is an anti epileptic Carbamazepine.<sup>9</sup> In a seven year study conducted by Devi, et al, anti epileptics like Carbamazepine are the most common cause of Stevens Johnson Syndrome especially in the first eight weeks of treatment in 80% of the cases.<sup>3</sup> Stevens Johnson Syndrome and Toxic Epidermal Necrolysis (TEN) are severe idiosyncratic reactions characterised by fever, mucocutaneous lesions leading to necrosis and sloughing of the epidermis. Depending upon the basal surface (BSA) involved, three entities are recognized:

- Stevens Johnson Syndrome- a minor form of Toxic Epidermal Necrolysis with less than 10% BSA involvement.
- Overlapping SJS/TEN- 10 to 30% of BSA involvement.
- TEN- more than 30% BSA involved.<sup>10</sup>

The mortality rate of SJS/TEN is high depending on the disease and its severity. It varies from 1-5% in SJS and 25-30% in TEN.<sup>11</sup> The severity of illness score for TEN(SCORTEN) is used widely for predicting the mortality of patients with SJS/TEN. This score consists of seven variables:

1. Age > 40 years
2. Skin detachment > 10% of BSA
3. Heart rate > 120/minute
4. Presence of malignancy
5. Blood Urea Nitrogen > 28mg/dl



6. Blood glucose level > 252mg/dl
7. Blood sodium bicarbonate levels < 20mEq/dl

Each variable gets 1 point if it is present. Higher the score of SCORTEN, higher is the mortality rate.<sup>12</sup> Lactate dehydrogenase levels (LDH) may also be considered in evaluation of the severity of the disease.<sup>13</sup>

At present, the exact mechanism of SJS is not known. A strong genetic predisposition has been found to be associated with SJS. It is believed to be associated with Human Leucocyte Antigen alleles (HLA B\*15:02).<sup>14,15</sup> SJS usually occurs during the first course of drug ingestion without prior sensitization.<sup>16</sup> Histopathological examination plays a crucial role in the diagnosis of SJS. Early histological finding in SJS is a perivascular mononuclear cell mainly T-lymphocytes which gathers around basal keratinocytes. In addition to medications, conditions such as malignancies, systemic lupus erythematosus, viral infection, exposure to ultraviolet rays may trigger SJS.<sup>17</sup>

The main therapeutic action in SJS is early recognition of the drug reaction and withdrawal of the drug because if delayed it can lead to serious complications. As such, there is no definitive treatment for acute SJS other than supportive care.<sup>18</sup>

According to the World Health Organization (WHO) system of causality definitions, the adverse drug reaction in this report case is categorized as 'Probable' with Naranjo Algorithm score of five. The adverse drug reaction was reported in Vigiflow (Worldwide Unique Number- 2017-58502 and AMC Report Number-BJGMC-Pune/Nov-2017/BBG-1860) Rechallenge was not carried out due to inherent risk involved.

This presentation of adverse reaction to Carbamazepine was thus seen in this case with fluid filled lesions and multiple discrete ulcers on the skin and thus involving both hepatic and renal systems.

## CONCLUSION

We report this case to aware physicians regarding drug implicated Stevens Johnson Syndrome which is a life-threatening reaction. So, judicious use of Carbamazepine is must to reduce mortality and morbidity.

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