Original Article **Case Report**

Carbamazepine-Induced Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis: A Clinical Case Report of a Rare Adverse Drug Reaction

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ABSTRACT: Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are rare but life-threatening skin reactions, often triggered by medications such as antiepileptic drugs, nonsteroidal anti-inflammatory drugs, and certain antibiotics. Carbamazepine is one of the most common antiepileptic medicine that causes SJS. A 13-year-old male with a history of 2 years of epilepsy presented with a painful rash and extensive blistering with mucous membrane involvement, along with fever and Nilkolsky sign. Based on clinical presentation and previous medication history, the patient was diagnosed with Stevens-Johnson syndrome, and carbamazepine was identified as the cause. Carbamazepine was discontinued, and the patient was given nutritional support, wound care, and intravenous fluids, along with steroid and antihistamine treatment. The patient's symptoms improved, and he was discharged after 13 days. Physicians must be aware of the potential for life-threatening drug hypersensitivity reactions in patients taking certain medications, particularly antiepileptic drugs. A thorough history and careful monitoring are essential for the early recognition and treatment of SJS and TEN. We want to advise all physicians that for patients with a previous drug reaction to this class of medication, carbamazepine prescribing should be avoided.

KEYWORDS: Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), carbamazepine (CBZ), phenytoin (PHT), ADR.

1. INTRODUCTION

Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN), defined by wide blisters arising on macules and atypical flat targets, are conditions with homogenous clinical characteristics and a potentially fatal consequence (1). Stevens–Johnson syndrome (SJS) is an immune-mediated disorder characterized by a prodromal illness followed by severe mucocutaneous symptoms (2). SJS and its more severe form, toxic epidermal necrolysis (TEN), are the result of a inflammatory response that results in keratinocyte necrosis and perivascular lymphocyte infiltration. Stevens–Johnson syndrome- poisonous epidermal necrolysis (SJS – TEN) imbrication has the characteristics of both SJS and TEN with the involvement of 10 – 30% of the body face area, epidermal detachment, pyrexia, and malaise. SJS was classically related to a drug hypersensitivity response; still, contagious etiologies are gradationally recognized as inciting agents (3). The prevalence of these responses is estimated to be 1.5 –8.3 cases per 1000000 person-year. The mortality from SJS is roughly 5 percent (7).

Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are both rare skin adverse drug reactions that are frequently actuated by particular medicines and can be life-threatening.

Antiepileptic drugs (AEDs), nonsteroidal anti-inflammatory drugs (NSAIDs), and certain antibiotics have been shown to activate these types of reactions (4).

Generally given ASMs, including carbamazepine (CBZ) and phenytoin (PHT), have been interlaced in life-threatening drug hypersensitivity responses (DHRs) that generally target the skin (5).

It affects all age groups, affecting further those individuals that have HIV, autoimmune conditions, immunocompromised cases, and those who have a beginning malignancy. Also, it's allowed to be an immune-mediated drug response with advanced rates in certain populations (6).

2. CASE PRESENTATION

A 13-year young male patient from Lucknow presented to a tertiary care hospital in Lucknow (UP), India with red colored painful rash initially over the forearm and then gradually spreaded all over the body (Figure 1).

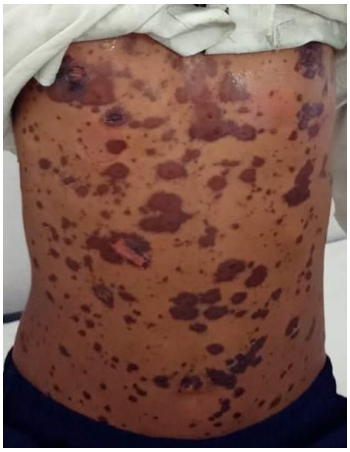

Figure 1 Rashes over whole abdomen at time of admission

The rash was present along with extensive blistering with mucous membrane involvement (Figure 2) associated with fever from day 1.

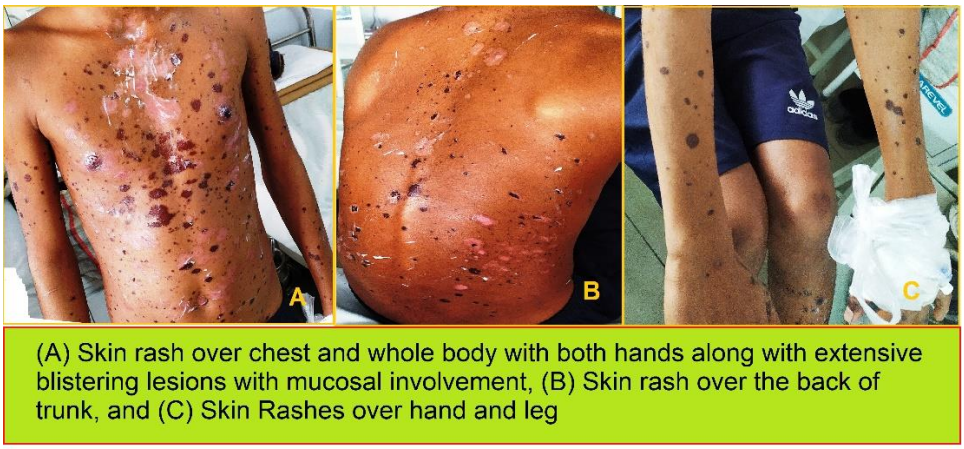

Figure 2 (A) Skin rash over the chest and whole body with both hands along with extensive blistering lesions with mucosal involvement, (B) Skin rash over the back of the trunk, and (C) Skin Rashes over hand and leg

There was presence of crusting over the lips. His eyelids and lips were swollen, and that was associated with blistering later on. There was presence of mouth ulcer (Figure 3) and genital involvement was also present. Nilkolsky sign was present (Figure 4).

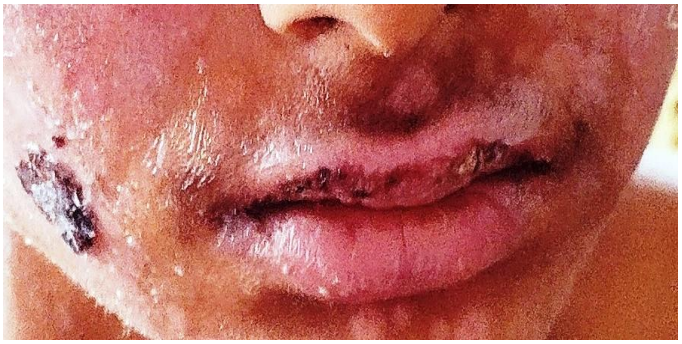

Figure 4 Mouth Ulcer on Lips

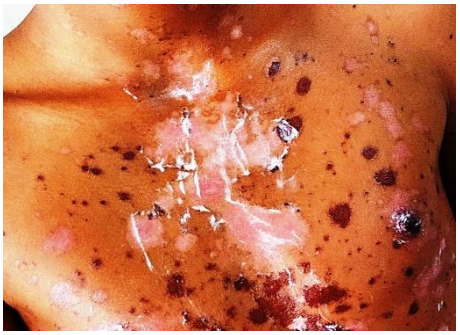

Figure 3 Nikolsky Sign

Patient also complains of odynophagia but he was able to swallow some liquids. He was first in his family to develop this type of reaction, there was no any significant family history and he had no any previous known allergy. A thorough review of the patient's medical history revealed that sodium valproate has been prescribed for her epilepsy since he was 11 years old. On peer pressure of society, he visited to his community medical practitioner, and he was switched to carbamazepine. After 5^{th} day of taking carbamazepine patient develops itching and rashes all over the body. On 9^{th} day patient condition became worse, and for that reason patient visited to tertiary care hospital.

To find out cause of SJS-TEN overlap, carbamazepine was stopped and 4mg dexamethasone and 25 milligrams of pheniramine maleate stat was given for preventing the patient from further complication of this reaction. After that his clinical symptom was improved.

The consultant evaluated and investigated the patient, and the following vitals were observed: HR-76BPM, RR-18 breath/minute, BP-100/70 mmHg, and Temp 100.2^{0}F. His laboratory investigations showed mildly elevated alanine transaminase (ALT), aspartate transaminase (AST), alkaline phosphatase (ALP), and C-reactive protein CRP, and mildly decreased serum creatinine. There was no sign and symptoms of infection was found as blood and urine test was negative. His complete blood count (CBC), electrolyte profile, random blood sugar, and viral markers was found to be normal. No skin biopsy was performed.

Laboratory Investigations

Table 2.1

BIOCHEMISTRY	
Serum Creatinine	0.35 mg/dl
Serum Urea	29.0 mg/dl
Liver Function Test	
Serum Bilirubin (Total)	0.3 mg/dl
SGPT/ALT	114.0 IU/L
SGOT/AST	48.0 IU/L
Alkaline Phosphatase	257.0 IU/L
Random Blood Sugar	99.0 mg/dl
C-Reactive Protein (CRP)	45.2
ELECTROLYTE PROFILE	
Serum Sodium (Na^+)	135.0 mmol/L
Serum Potassium (K^+)	3.6 mmol/L
Ionic Calcium (I. Ca^{++})	1.23 mmol/L
HEMATOLOGY	
Complete Blood Count	
Hemoglobin (Hb)	12.0 gm%
Total Leucocyte Count (TLC)	5,800 cu/mm
Differential Leucocyte Count	
Neutrophils	48%
Lymphocytes	42%
Eosinophils	08%
Monocytes	02%
RBC	3.64 x 10/ul
HCT	33.7%
MCV	92.6 fL
MCH	33.1 pg
MCHC	35.1 g/dL
RDW	12.7%
Platelet Count	1.90 Lac/cumm

Based on his clinical presence and previous medication the patient was presumed diagnosed as Stevens–Johnson syndrome-toxic epidermal necrolysis (SJS-TEN) and the cause of SJS-TEN was found to be the rare adverse drug reaction of carbamazepine.

The patient was admitted in emergency ward and carbamazepine was immediately discontinued; immediately the patient received nutritional support as multivitamins, eye care, wound care, and intravenous fluids (like NS and Paracetamol) for maintaining positive balance. In eye care, Zymer eye drop (Gatifloxacin 0.3% w/v) and Refresh Tears Eye Drop was given and in wound care, Cosvate G Cream [Clobetasol (0.05% w/w) + Gentamicin (0.1% w/w)], Mucopain Gel (Benzocaine 20% w/w), Oraways Oral Paste (Triamcinolone 0.1% w/w), Betadine mouth wash, azithromycin, and Q-Sone Cream (Fluticasone Propionate 0.05% w/w) was given. For his epilepsy, tablet Valproate [Sodium Valproate (200mg) + Valproic Acid (87mg)] was continued.

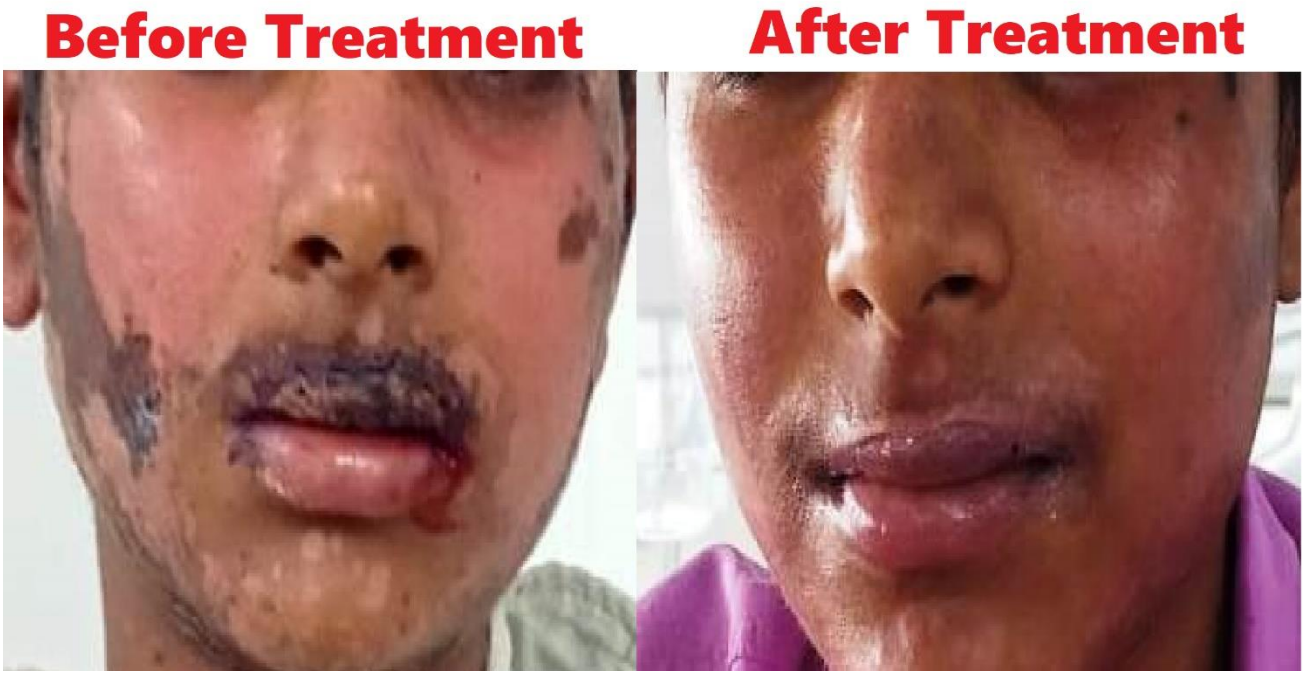

Figure 5 Before and After Treatment

The steroid treatment was given in the form of 4 milligrams of dexamethasone intravenously once daily along with an antihistaminic drug in the form of 22.75 milligrams of pheniramine maleate intravenously two time a day (for itching) for 7 days. The patient got better and was discharged in good general condition after 13 days (Figure 5).

3. DISCUSSION

The case presented in this report highlights the importance of monitoring patients closely for adverse effects of antiepileptic drugs, particularly carbamazepine, and promptly recognizing and managing such effects to prevent further complications.

Carbamazepine is a widely used antiepileptic drug that can cause a range of adverse effects, including skin reactions, hepatotoxicity, and hematologic abnormalities. Among these, SJS/TEN is a rare but potentially life-threatening skin reaction that can occur with carbamazepine use. This adverse reaction is characterized by a widespread rash, blistering, and mucosal involvement and can progress rapidly to involve large areas of the body, leading to significant morbidity and mortality.

Therefore, early recognition and discontinuation of the offending drug are critical to prevent further damage.

Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are severe cutaneous reactions characterized by widespread skin detachment and mucosal involvement. The condition is often caused by exposure to certain medications, particularly antiepileptic drugs (AEDs) and antibiotics.

In the present case, the patient had a previous history of epilepsy and was taking carbamazepine from past 9 day for the same before admission. The development of the rash and mucosal involvement after exposure to carbamazepine strongly suggests a drug-induced hypersensitivity reaction.

The patient was admitted to the emergency ward with symptoms of fever, sore throat, and widespread rash, which were consistent with a diagnosis of SJS/TEN. Carbamazepine was immediately discontinued, and the patient was managed with supportive care, including nutritional support, eye care, wound care, and intravenous fluids. The patient was also started on the tablet Valproate for his epilepsy, which was continued.

The management of SJS/TEN requires a multidisciplinary approach involving dermatologists, intensivists, ophthalmologists, and nutritionists. Patients with SJS/TEN require close monitoring in the intensive care unit, and the management should be tailored to the individual patient's needs. In this case, the patient received multidisciplinary care, which contributed to the favorable outcome.

SJS-TEN is a spectrum of disease, with SJS representing the milder end and TEN representing the more severe end. The condition is diagnosed based on clinical features and a history of medication exposure. The characteristic rash begins as erythematous macules that rapidly progress to form bullae and detachments of the epidermis. Mucosal involvement is common and can occur in the eyes, mouth, and genitalia. In the present case, the patient had extensive blistering with mucous membrane involvement and crusting over the lips. The presence of the Nilkolsky sign is a characteristic finding of SJS-TEN and is defined as the separation of the epidermis from the dermis with slight pressure. Stevens–Johnson syndrome and toxic epidermal necrolysis (SJS/TEN) belongs to type B class of adverse drug reactions [8], and It is a hypersensitivity reaction of type IV (subtype C) that typically affects the skin and mucous membranes [9].

The management of SJS/TEN requires a multidisciplinary approach involving dermatologists, intensivists, ophthalmologists, and nutritionists. Patients with SJS/TEN require close monitoring in the intensive care unit, and the management should be tailored to the individual patient's needs. In this case, the patient received multidisciplinary care, which contributed to the favorable outcome.

The management of SJS/TEN involves a multidisciplinary approach, with close monitoring of vital signs, fluid and electrolyte balance, nutritional status, wound care, and pain management. In

addition, systemic corticosteroids and immunoglobulins have been used in the treatment of SJS/TEN, although their efficacy remains controversial. The use of topical agents such as corticosteroids, antibiotics, and analgesics can also be helpful in managing skin and mucosal symptoms.

In the present case, the patient was given 4 milligrams of dexamethasone intravenously once daily along with an antihistaminic drug (for itching) in the form of 22.75 milligrams of pheniramine maleate intravenously twice daily for 7 days. The patient showed improvement with this treatment, and after 13 days, he was discharged in good general condition.

4. CONCLUSION

Carbamazepine is one of the common drugs that can result in SJS, and a thorough history must be taken if carbamazepine medication is clinically necessary. Any patient who has experienced a drug reaction in the past should be avoided by physicians in prescribing carbamazepine. It is crucial to promptly discontinue the offending drug and provide appropriate medical care to manage the symptoms of SJS-TEN overlap. Supportive care, including nutritional support, wound care, and intravenous fluids, should also be provided. The use of systemic corticosteroids remains controversial, and their use should be individualized based on the severity of the disease and the patient's clinical status. With proper management, patients can recover from SJS-TEN and return to good health.

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Author contributions

All authors have accepted responsibility for the entire content of this manuscript and approved its submission.

Conflicts of interests

Authors state no conflict of interest.

Data availability

The patient’s data have not been made public. They are kept with all the authors. If anyone need this data then request to corresponding author via e-mail.

Ethics approval

The subject gave informed consent for participating in the study.

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