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Case Series

A Case Series on Antiepileptic Drug–Induced Stevens–Johnson Syndrome in a Tertiary Care Centre of Jharkhand

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Abstract

Background: Stevens–Johnson Syndrome (SJS) is a rare but potentially life-threatening mucocutaneous hypersensitivity reaction commonly triggered by medications, particularly antiepileptic drugs (AEDs). Anticonvulsants such as carbamazepine and phenytoin are well-recognized causes, while sodium valproate is less frequently implicated. Early identification and prompt withdrawal of the offending drug are crucial for favorable outcomes.

Methodology: This descriptive case series included three male patients who developed Stevens–Johnson Syndrome after exposure to antiepileptic drugs. Clinical history, drug details, temporal association, laboratory findings, management, and outcomes were documented. Diagnosis was based on characteristic mucocutaneous features. The suspected drugs were promptly withdrawn, supportive treatment was given, and causality was assessed using WHO-UMC criteria.

Case Presentation: We report a case series of three male patients aged 20–62 years who developed severe cutaneous adverse reactions following exposure to sodium valproate, carbamazepine, and phenytoin. The latency period ranged from 2 days to 2 weeks after initiation of therapy. Clinical manifestations included fever, generalized erythematous and bullous eruptions, mucosal erosions, ocular involvement, and skin peeling suggestive of SJS. Laboratory investigations were largely within normal limits, except for mild elevation of hepatic enzymes in the carbamazepine case. All suspected drugs were immediately withdrawn, and patients were managed with hospitalization, intravenous fluids, antibiotics, skin emollients, eye care, and supportive therapy. Causality assessment using WHO-UMC criteria categorized all cases as "Probable." All patients showed clinical improvement and were discharged in recovering condition.

Conclusion: This case series reinforces the continued risk of SJS with antiepileptic drugs, particularly during the early phase of therapy. Vigilant monitoring, early recognition of warning signs, and prompt discontinuation of the suspected drug are essential to prevent severe complications and improve patient outcomes.

Keywords : Stevens–Johnson Syndrome; Severe Cutaneous Adverse Reactions; Antiepileptic Drugs; Carbamazepine; Phenytoin; Sodium Valproate; Drug Hypersensitivity.

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Introduction

Stevens–Johnson Syndrome (SJS) is a rare but serious and potentially life-threatening mucocutaneous disorder characterized by extensive epidermal necrosis, skin detachment, and involvement of mucous membranes. It is considered a severe form of adverse drug reaction and represents an important medical emergency due to its high morbidity and mortality. Although the estimated annual incidence is approximately 5 cases per million population, the clinical impact is significant because of the severity of the condition and the need for intensive management.[1,2]Among the various causes, medications are the most common trigger of SJS, particularly antiepileptic drugs (AEDs). Anticonvulsants such as carbamazepine, phenytoin, and phenobarbital have been frequently implicated. Carbamazepine and phenytoin are well-established causes of drug-induced SJS, whereas reports related to newer agents like oxcarbazepine are comparatively fewer. However, available data suggest that oxcarbazepine can also precipitate SJS, with an estimated incidence of 5–6 cases per million persons per year.[3]The exact mechanism

underlying AED-induced SJS is not completely understood, but immunological and genetic factors are believed to play an important role. Studies have demonstrated a strong association between certain human leukocyte antigen (HLA) alleles, particularly HLA-B*1502, and an increased risk of SJS in Asian populations receiving antiepileptic drugs.[4] This genetic predisposition highlights the importance of careful drug selection and monitoring, especially in susceptible individuals.

In this case series, we describe patients who developed SJS following exposure to antiepileptic medications at a tertiary care centre in Jharkhand. The objective is to analyze the clinical presentation, causative drugs, management strategies, and outcomes, thereby contributing to increased awareness and early recognition of this severe adverse drug reaction.

Materials and Methods

Study Design: This study was conducted as a descriptive case series of patients who developed suspected adverse drug reactions (ADRs) following administration of anticonvulsant medications. The cases were reported under the Pharmacovigilance Programme of India (PvPI) using the Suspected Adverse Drug Reaction Reporting Form.

Study Setting: The study was conducted at Rajendra Institute of Medical Sciences (RIMS), Ranchi, a tertiary care teaching hospital. All patients presented to the Emergency Department and were subsequently admitted for further evaluation and management.

Study Duration: The cases included in this series were reported between August 2025 and January 2026.

Study Population: The study included three male patients aged 20–62 years who developed severe cutaneous adverse drug reactions following administration of anticonvulsant medications (sodium valproate, carbamazepine, and phenytoin).

Inclusion Criteria

- Patients of any age and gender.
- Patients who developed suspected cutaneous adverse drug reactions following initiation of anticonvulsant therapy.
- Cases reported to the Adverse Drug Reaction Monitoring Centre (AMC).
- Patients requiring hospitalization for management.

Exclusion Criteria

- Patients with incomplete clinical records.
- Cutaneous reactions attributable to infections or other identifiable non-drug causes.
- Patients with known pre-existing dermatological disorders mimicking drug reactions.

Data Collection

Data were collected from:

- Suspected ADR Reporting Forms (PvPI format)
- Patient case records
- Clinical examination findings
- Laboratory investigation reports

The following details were recorded:

- Demographic profile (age, gender)
- Detailed drug history (name, dose, frequency, duration, indication)
- Time interval between drug initiation and onset of reaction
- Clinical features of adverse reaction
- Relevant medical history and comorbidities
- Laboratory parameters (hemoglobin, liver function tests, renal function tests)
- Management details
- Outcome of the reaction

Assessment of Adverse Drug Reaction

1. Causality Assessment: Causality was assessed using the WHO–UMC (World Health Organization–Uppsala Monitoring Centre) causality assessment scale.

Based on temporal association, dechallenge response, and absence of alternative explanations, all cases were categorized as “Probable.”

2. Seriousness Assessment: Seriousness of ADR was determined as per PvPI guidelines. The reactions were categorized as “Serious” as they required hospitalization and were medically important conditions (Stevens–Johnson Syndrome).

3. Severity Assessment

Clinical severity was assessed based on:

- Extent of skin involvement
- Presence of mucosal involvement
- Systemic symptoms
- Requirement of inpatient care

Investigations: All patients underwent routine laboratory investigations including:

- Complete blood count
- Liver function tests (SGOT, SGPT, total bilirubin)
- Renal function tests (serum urea, serum creatinine)

Additional supportive investigations were performed as clinically indicated.

Management Protocol: Upon suspicion of drug-induced reaction:

1. The suspected offending drug was immediately withdrawn.
2. All non-essential medications were discontinued.
3. Patients were admitted for monitoring.
4. Supportive management was initiated, including:

    - Intravenous fluids
    - Systemic antibiotics (where indicated)
    - Skin emollients
    - Eye care
    - Symptomatic treatment

Patients were monitored for clinical improvement and complications during hospitalization.

Ethical Considerations: Patient confidentiality was strictly maintained. Identifying information was anonymized. The cases were reported under the Pharmacovigilance Programme of India as part of routine ADR monitoring.

Case Report

Case 1: A 62-year-old male, known case of chronic obstructive pulmonary disease (COPD) for the past two years, with no history of diabetes mellitus, hypertension, or known drug allergies, presented with complaints of fever and progressive skin rash. The patient had recently developed a seizure disorder and attended a private clinic on 18/08/2025, where he was prescribed oral sodium valproate (Valpin®, Lupin) 500 mg twice daily. After approximately two weeks of therapy, he developed fever followed by erythematous skin rash. Despite treatment with antihistamines, his symptoms worsened, and he subsequently developed generalized bullous skin eruptions along with painful oral lesions. The clinical presentation was suggestive of Stevens–Johnson Syndrome (SJS). The suspected drug was discontinued on 01/09/2025. The patient presented to the Emergency Department of RIMS, Ranchi, on 05/09/2025 for further management.

Laboratory investigations performed on 04/09/2025 revealed hemoglobin of 13 g/dL, total bilirubin 1.2 mg/dL, SGOT 39 U/L, SGPT 40 U/L, serum urea 20 mg/dL, and serum creatinine 1.2 mg/dL.

The patient was admitted, and the offending drug was withdrawn. All non-essential medications were discontinued. He was managed conservatively with intravenous fluids, systemic antibiotics, skin emollients, eye care, and supportive therapy. Concomitant medications included Deriphyllin (oral, BD) and Budecort inhaler 200 mcg (BD), both started on 10/01/2025 for COPD management.The reaction was classified as a serious, medically important condition. Causality assessment was considered “Probable.” The patient showed gradual clinical improvement and was recovering at the time of reporting.

Figure 1:

Case 2: A 20-year-old male with a history of substance abuse for one year presented with withdrawal symptoms. He was started on oral carbamazepine 200 mg twice daily on 15/11/2025 at a private clinic for management of withdrawal symptoms. Two days after initiation of therapy, the patient developed erythema over the neck and face, which gradually progressed to involve the entire body.

The rash was associated with itching. Despite continuation of therapy initially, the symptoms worsened, and the drug was discontinued on 12/12/2025. The patient presented to the Emergency OPD at RIMS, Ranchi, on 13/12/2025

for further evaluation and management. Laboratory investigations on 13/12/2025 revealed hemoglobin of 13 g/dL, total bilirubin 1.2 mg/dL, SGOT 88 U/L, SGPT 82 U/L, serum urea 20 mg/dL, and serum creatinine 1.2 mg/dL. The patient was admitted, and the suspected drug was withdrawn. All non-essential medications were discontinued. He was managed with intravenous fluids, antibiotics, skin emollients, eye care, and other supportive treatment. The adverse drug reaction was considered serious. Causality assessment was categorized as "Probable." The patient improved with supportive management and was recovering at the time of reporting.

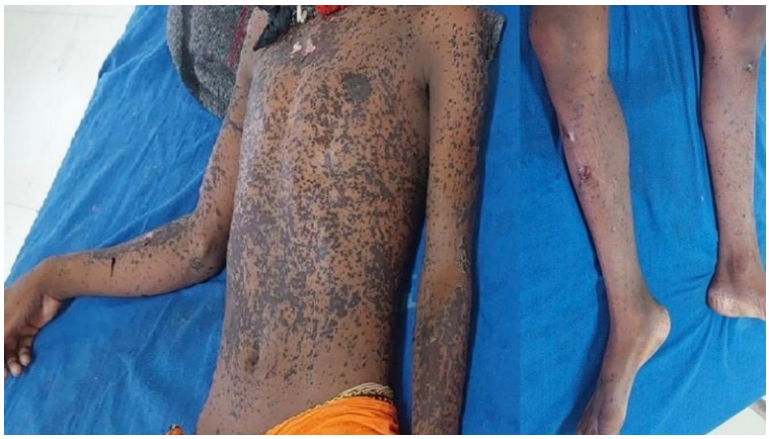

Figure 2:

Case 3: A 34-year-old male with a known seizure disorder of one month duration attended a private clinic on 18/11/2025 and was started on oral phenytoin (Eptoin®) 100 mg three times daily. Approximately 10 days after initiation of therapy, he developed erythema over the neck and face, which gradually spread over the body. He subsequently developed painful oral lesions, mucosal erosions, redness of the eyes, and skin peeling with blister formation. The clinical features were suggestive of Stevens–Johnson Syndrome (SJS). The suspected drug was discontinued on 03/12/2025, and the patient presented to the Emergency Department of RIMS, Ranchi, for further management. Investigations performed on 03/12/2025 revealed hemoglobin of 12 g/dL, total bilirubin 1.2 mg/dL, SGOT 48 U/L, SGPT 44 U/L, and serum creatinine 1 mg/dL. There was no history of tuberculosis, hypertension, or known drug allergies. The patient was admitted, and the offending drug was withdrawn. Non-essential medications were discontinued. He was managed with systemic antibiotics, skin emollients, eye care, and supportive measures.

The adverse drug reaction was categorized as serious. Causality assessment was "Probable." The patient showed clinical improvement with treatment and was recovering at the time of reporting.

Figure 3:

Table 1: Clinical Profile of Anticonvulsant-Induced Adverse Drug Reactions

Parameter	Case 1	Case 2	Case 3
Patient Initials	K I	S K	M I
Age / Gender	62 years / Male	20 years / Male	34 years / Male
Underlying Condition	COPD (2 years), newly diagnosed seizure disorder	Substance abuse (1 year)	Seizure disorder (1 month)
Suspected Drug	Sodium Valproate (Valpin®)	Carbamazepine	Phenytoin (Eptoin®)
Manufacturer	Lupin	Sun Pharma	Solus (Generic)
Dose & Frequency	500 mg BD	200 mg BD	100 mg TDS
Route	Oral	Oral	Oral
Therapy Duration	18/08/2025 – 01/09/2025	15/11/2025 – 13/12/2025	18/11/2025 – 03/12/2025
Indication	Seizure	Withdrawal symptoms	Seizure
Onset of Reaction	After ~2 weeks	After 2 days	After 10 days
Date of Onset	18/08/2025	13/12/2025	18/11/2025
Clinical Features	Fever, generalized bullous eruptions, oral lesions suggestive of SJS	Erythema over neck & face progressing to generalized rash with itching	Erythema, generalized rash, oral lesions, mucosal erosions, eye redness, skin peeling with blistering suggestive of SJS
Laboratory Findings	Hb 13 g/dL; TB 1.2 mg/dL; SGOT 39 U/L; SGPT 40 U/L; Urea 20 mg/dL; Creatinine 1.2 mg/dL	Hb 13 g/dL; TB 1.2 mg/dL; SGOT 88 U/L; SGPT 82 U/L; Urea 20 mg/dL; Creatinine 1.2 mg/dL	Hb 12 g/dL; TB 1.2 mg/dL; SGOT 48 U/L; SGPT 44 U/L; Creatinine 1 mg/dL
Relevant Medical History	No DM/HTN; No known drug allergy	Substance abuse	No TB/HTN; No known drug allergy
Seriousness	Serious (Medically important condition)	Serious	Serious
Action Taken	Drug withdrawn	Drug withdrawn	Drug withdrawn
Management	Admission, IV fluids, antibiotics, skin emollients, eye care, supportive therapy	Admission, IV fluids, antibiotics, skin emollients, eye care, supportive therapy	Admission, antibiotics, skin emollients, eye care, supportive therapy
Concomitant Drugs	Deriphyllin (BD), Budecort inhaler 200 mcg (BD)	None reported	None reported
Causality Assessment	Probable	Probable	Probable
Outcome	Recovering	Recovering	Recovering

Discussion

Stevens–Johnson Syndrome (SJS) is a rare but potentially life threatening mucocutaneous hypersensitivity reaction characterized by epidermal necrosis, mucosal erosions, and systemic involvement. Antiepileptic drugs (AEDs), particularly anticonvulsants, remain among the most frequently implicated causes of severe cutaneous adverse reactions (SCARs). The findings in the present case series involving sodium valproate, carbamazepine, and phenytoin are consistent with existing literature.

The EuroSCAR study (Mockenhaupt et al., 2005) demonstrated a significantly increased risk of SJS/TEN with carbamazepine and phenytoin, especially during the first eight weeks of therapy. In our series, the patients receiving carbamazepine and phenytoin developed cutaneous reactions shortly after drug initiation, supporting the strong association between AEDs and SJS. The latency period observed ranged from 2 days to 2 weeks, which is comparable to previous reports by Rzany et al. (1999) and Mockenhaupt et al. (2005), identifying the first 1–3 weeks as the highest risk period. The very early onset in one patient may reflect heightened individual susceptibility. Genetic predisposition plays an important role in AED-induced SJS. Chung et al. (2004) established a strong association between carbamazepine-induced SJS and the HLA-B*1502 allele in Asian populations, and current pharmacogenomic recommendations emphasize HLA screening before initiating carbamazepine in high-risk groups. Although genetic testing was not performed in our patients, the clinical presentation is consistent with immune-mediated mechanisms influenced by genetic susceptibility. Sodium valproate is generally considered to carry a lower risk compared to anticonvulsants; however, rare cases of valproate-associated SJS have been documented. In the present series, one patient developed

classical features of SJS approximately two weeks after starting valproate, indicating that even AEDs cannot be considered entirely risk-free. Clinically, mucosal involvement, bullous lesions, and ocular symptoms observed in our patients align with established diagnostic criteria described by Bastuji-Garin et al. (1993). None of the patients progressed to multiorgan failure, likely due to early recognition and prompt discontinuation of the offending drug. Previous studies, including Schwartz et al. (2013), have shown that early drug withdrawal significantly improves prognosis. Overall, this case series reinforces the continued relevance of anticonvulsant-induced SJS in clinical practice. Careful monitoring during the initial weeks of therapy, awareness of pharmacogenetic risk factors, and early recognition of warning signs remain essential to reduce morbidity and mortality associated with this serious adverse drug reaction.

Conclusion

This case series highlights three instances of antiepileptic drug–associated Stevens–Johnson Syndrome (SJS) occurring in male patients exposed to sodium valproate, carbamazepine, and phenytoin. The reactions developed within a short latency period ranging from 2 days to 2 weeks after initiation of therapy, emphasizing the high-risk window during the early phase of treatment. Anticonvulsants (carbamazepine and phenytoin) demonstrated rapid onset and classical mucocutaneous manifestations, while sodium valproate, though comparatively safer, was also implicated. All cases were classified as “Probable” based on WHO-UMC causality assessment and showed clinical improvement following prompt drug withdrawal and supportive management. These findings underscore the importance of early recognition, immediate discontinuation of the suspected drug, and vigilant monitoring during the initial weeks of antiepileptic therapy to reduce morbidity and prevent life-threatening complications.

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