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Medical Negligence Leading to the Onset of Stevens-Johnson Syndrome: A Case Report

Kimia Kazemi

ABSTRACT

INTRODUCTION AND IMPORTANCE

Stevens-Johnson Syndrome (SJS) is a life-threatening, drug-induced hypersensitivity reaction with high morbidity and mortality. This case report demonstrates the critical importance of thorough history-taking and antibiotic stewardship, as a preventable drug-drug interaction between lamotrigine and azithromycin led to SJS in a young patient. The case exposes dangerous shortcomings in standard practice protocols that jeopardize patient outcomes.

CASE PRESENTATION

A 16-year-old female on lamotrigine for depressive episodes presented to the emergency room with fever (40°C), extensive mucocutaneous erosions, and respiratory distress after taking azithromycin for flu-like symptoms. Clinical diagnosis of SJS (<10% total body surface area involvement) was confirmed by Nikolsky's sign, bullae, and mucosal lesions. She required intubation and multidisciplinary management, including ophthalmologic intervention for corneal involvement.

CLINICAL DISCUSSION

The case reveals two critical errors: (1) failure to reconcile the patient's lamotrigine use (a known SJS trigger) before prescribing azithromycin, and (2) inappropriate antibiotic use for a likely viral infection. Comparable cases emphasize lamotrigine's interaction risks and the need for clinician education.

CONCLUSION

This preventable case calls for strict adherence to medication reconciliation protocols, antibiotic stewardship, and patient education about high-risk drugs. Systemic interventions, such as electronic health record alerts for drug interactions, could mitigate future occurrences.

Keywords: Steven Johnson Syndrome, Drug-drug interaction, Lamotrigine, Azithromycin, Medical negligence

Introduction

Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are considered a delayed-type hypersensitivity reaction to drugs. They represent true medical emergencies, and early recognition and appropriate management are decisive for survival. SJS and TEN manifest with an "influenza-like" prodromal phase (malaise, fever), followed by painful cutaneous and mucous membrane (ocular, oral, and genital) lesions, and other systemic symptoms.¹

TEN and SJS are classified according to the percentage of total body surface area (TBSA) affected:

- SJS (<10% of TBSA)
- TEN/SJS overlap (10–30% of TBSA)
- TEN (>30% of TBSA)²

These rare conditions reportedly affect patients in all age groups, with incidences of approximately two to seven cases per million people annually.²

Characteristically, they manifest with extensive mucosal and epidermal erosion and necrosis and can be observed as a result of keratinocyte death. This, in turn, results in considerable fluid loss, susceptibility to infection and sepsis, as well as organ dysfunction, which may explain the high mortality rates of up to 75%.²

The dermal erosions observed in TEN/SJS patients resemble second-degree burn wounds.² Consequently, these patients may initially be mistaken for burn victims. Given the frequent multi-organ involvement, multidisciplinary care—including dermatology, ophthalmology, and critical care—is essential for optimal management.

Methods

This case report adheres to the CARE (CAse REports) guidelines for transparent and complete case reporting.³

Case Report

A 16-year-old female presented to the emergency room semi-conscious, with her mother. Clinical findings included:

- Fever (40°C)
- Erythematous rash, swollen lips, and tongue
- O₂ saturation of 91%, progressing to airway constriction (requiring intubation)
- Nikolsky's sign positive, with bullae on the trunk and upper extremities

History revealed the patient had taken two doses of azithromycin for flu-like symptoms. The mother reported recent antidepressant use, later identified as lamotrigine.

- **Clinical Diagnosis:** SJS (<10% TBSA) based on mucosal lesions and bullae
- **Differential Diagnoses:** Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) syndrome, staphylococcal scalded skin syndrome (ruled out by history and presentation)

Treatment

The patient was initially managed in the emergency department for 72 hours, during which she remained unconscious with a persistent fever (40°C) but was hemodynamically stable. Given her skin erosions and concerns about secondary infections, a sterile unit was medically necessary. Upon availability of a sterile

isolation room in the dermatology ward, she was transferred for specialized care. A multidisciplinary team collaborated to optimize her treatment regimen (Table 1).

Table 1 | Timeline of clinical phases and key events

Timeline	Clinical Phase	Key Events
Day 0	Initial Outpatient Care	- Azithromycin dose 1 prescribed for flu symptoms - Patient on lamotrigine for depression
Day 0.5	Outpatient Deterioration	- Azithromycin dose 2 administered - Initial rash development - Patient reports malaise
Day 1	ER Admission	- Fever (40°C), mucosal involvement, hypoxia - SJS suspected
Day 1–3	ER Care	- Patient unconscious - Intubation - Progressive epidermal detachment
Day 4–18	Inpatient Care	- Regained consciousness (Day 4) - Vision complications - Ocular involvement noted - Stabilization of skin lesions
Week 3–8	Outpatient Recovery	- Weekly dermatology follow-ups - Persistent photosensitivity - Hair/nail loss
Month 3	Final Follow-Up	Full epithelialization achieved Visual acuity 20/20 bilaterally No residual scarring Hair/nail regrowth



Fig 1 | Acute mucocutaneous involvement in Stevens-Johnson syndrome (SJS). Erythematous macules with central necrosis on the trunk and oral mucosa



Fig 2 | Peripheral peeling of necrotic epidermis at lesion margins, resembling tissue paper-like folds

Therapeutic Interventions

- Antimicrobial prophylaxis consisted of daily potassium permanganate baths supplemented with parenteral broad-spectrum antibiotics.
- Daily wound care included drainage of large bullae and topical zinc peroxide application to erosions.
- Upon regaining consciousness, the patient reported visual loss (“Please turn on the lights”). Examination revealed bilateral corneal and conjunctival lesions, prompting urgent transfer to a tertiary ophthalmology center for specialized care.

Recovery Phase

The patient required 18 days of hospitalization, during which she received:

- Immunosuppressive therapy
- Aggressive electrolyte repletion
- Nutritional support

Outcome and Follow-Up

By day 18 of hospitalization, the patient’s condition had stabilized, and she was deemed medically fit for discharge. After discussing the option of continuing recovery at home, the patient and her family agreed, and discharge planning was initiated.

Post-discharge care included:

- Weekly dermatology evaluations for 8 weeks
- Strict photoprotection measures (SPF 50+, UPF 50+ clothing, indoor confinement)

The patient experienced transient alopecia and onycholysis, with complete regrowth observed in 3 months. The patient achieved a full recovery with no long-term morbidity (Figures 1, 2, 3, 4, 5, and 6).

Discussion

Lamotrigine is an antiepileptic medication that is also used as a mood stabilizer.⁴ There are many adverse side effects associated with the use of lamotrigine. Side effects may include nausea or vomiting, irritability, visual disturbances, headaches, insomnia, dizziness, tremors, agitation, and conjunctivitis. More serious side effects of lamotrigine involve serious skin conditions such as Stevens-Johnson Syndrome, TEN, and DRESS.⁵

Although lamotrigine alone did not cause a reaction, its combination with azithromycin (a typically safe antibiotic⁶) likely induced a drug-drug interaction that provoked a delayed hypersensitivity reaction.

Drugs are the etiologic factor in the majority of SJS/TEN cases. However, it is still unknown how a certain drug may actually induce epidermal necrosis. T cells, especially CD8+ lymphocytes, have been identified to play an important role in the process that is most likely mediated by cytokines.⁷ The main cytokine associated with blisters in patients is CD8+ T cells.⁷

The mechanism of action of lamotrigine in inducing SJS is under debate. However, it has been proposed that, since its metabolism is mainly hepatic through

glucuronidation by UGT1A4 and UGT2B7, certain genetic variations in these enzymes would compromise the clearance of the drug, increasing its serum concentrations.⁸

The chance of developing Stevens-Johnson syndrome after use of lamotrigine remains low, but it should be known to physicians as a possible adverse effect while prescribing the medication.

The patient reported a history of depressive episodes with no prior manic or hypomanic symptoms, calling into question the rationale for initiating a mood stabilizer, a class of medications primarily indicated for bipolar disorder.⁹ This clinical decision warrants further scrutiny, particularly regarding whether alternative first-line treatments with safer profiles might have been more appropriate.

The case also highlights two concerning clinical lapses: (1) the physician's failure to elicit the patient's medication history, and (2) inappropriate azithromycin prescription for suspected viral infection, a clear deviation from antimicrobial stewardship guidelines.¹⁰ This raises critical questions about whether this represents

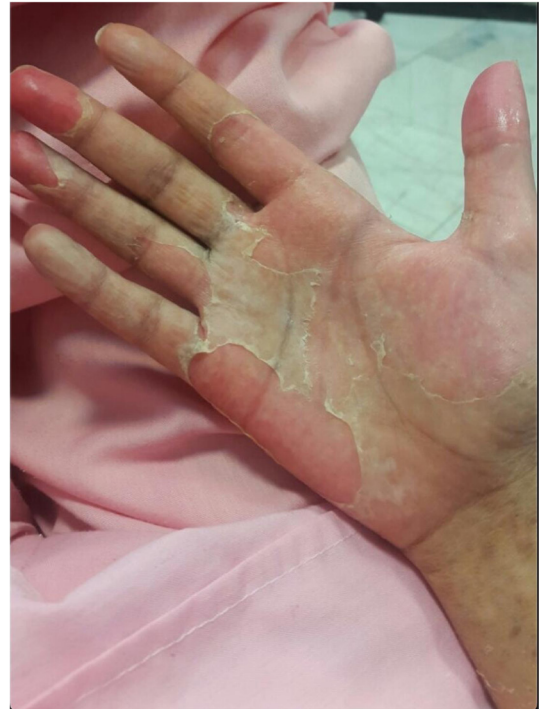


Fig 5 | Large sheets of necrotic epidermis peeled from fingertips to wrists, resembling wet tissue paper detachment



Fig 3 | Post-inflammatory hyperpigmentation and necrosis developed on the bilateral lower extremities



Fig 4 | Thin-walled vesicles on the trunk and extremities ruptured spontaneously, revealing painful erosions with a glazed appearance



Fig 6 | Dorsal hands showed darker pigmentation than palms, suggesting UV-sensitized melanocyte activation

an individual knowledge gap or reflects broader regional prescribing patterns for viral illnesses.

Addressing these practice gaps through improved clinician education and standardized protocols may:

1. Enhance patient safety by preventing similar adverse drug events
2. Reduce unnecessary hospitalizations
3. Lower healthcare burdens associated with preventable complications

Conclusion

This case of lamotrigine-azithromycin-induced SJS highlights critical vulnerabilities in clinical practice that demand urgent attention. The case underscores the fundamental importance of meticulous history-taking, where every medication detail must be proactively elicited to avoid dangerous interactions.

While SJS literature extensively covers anticonvulsant interactions, this case highlights azithromycin as an underrecognized trigger when combined with lamotrigine. Our findings underscore that preventable errors (e.g., incomplete medication reconciliation) remain prevalent, undermining patient safety.

Physicians must recognize their responsibility to ensure patients and caregivers fully understand potential adverse effects when prescribing high-risk medications like lamotrigine, particularly when combined with other common drugs.

The broader implications extend beyond individual practice. Systemic failures, including the persistent overprescription of antibiotics for viral infections and the lack of robust drug interaction alerts, create perfect conditions for similar adverse events.

Antimicrobial stewardship programs and enhanced electronic health record safeguards could significantly mitigate these risks.

While our patient ultimately achieved full recovery, the harsh reality remains that SJS carries a 10–15% mortality rate, with many survivors facing lifelong disabilities such as vision loss or chronic pain. This is a reminder that what was a near-miss in this case could easily be fatal in another. The case also exposes significant gaps in our understanding of SJS pathophysiology. Despite being first described over a century ago, key questions about its immunologic triggers and risk stratification remain unanswered. We urgently need mechanistic studies, evidence-based

monitoring guidelines, and international registries to track drug-associated cases.

To prevent future occurrences, we urgently recommend:

1. Mandatory medication safety training for all practitioners, emphasizing high-risk drug interactions
2. Development of patient-accessible digital tools (e.g., medication interaction apps) to facilitate active participation in treatment safety
3. Increased funding for SJS research to develop predictive biomarkers and targeted therapies

As the patient herself later reflected, “I never knew my antidepressant could interact with antibiotics.” This simple statement encapsulates the profound need for better communication at all levels of care.

While this case resulted in full recovery, it stands as a critical reminder to healthcare teams of the potentially fatal consequences of overlooked drug interactions.

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