Case Report

Amoxicillin–Clavulanic Acid Induced Stevens–Johnson Syndrome and Toxic Epidermal Necrolysis Overlap: A Case Report

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ABSTRACT

Stevens–Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are rare, life-threatening, severe cutaneous adverse reactions, and amoxicillin–clavulanic acid is an uncommon trigger. A 64-year-old man with HIV on abacavir-based antiretroviral therapy developed widespread targetoid erythematous-to-dusky lesions, epidermal peeling, and painful oral erosions after recent exposure to oral amoxicillin–clavulanic acid. Skin biopsy showed epidermal ulceration and necrosis with basal vacuolar change and dyskeratotic cells, consistent with toxic epidermal necrolysis. Epidermal detachment involved approximately 25%–30% body surface area, confirming SJS–TEN overlap. Amoxicillin–clavulanic acid was considered the most likely offending drug based on temporal association and a probable Naranjo score of 6. SCORTEN was 2. The patient was managed with prompt drug withdrawal, supportive care, corticosteroids, intravenous immunoglobulin, and cyclosporine, with subsequent clinical improvement. This case highlights the need for early recognition and pharmacovigilance reporting of rare but severe antibiotic-associated reactions.

Keywords: Stevens–Johnson syndrome, toxic epidermal necrolysis, SJS-TEN overlap, amoxicillin-clavulanate, pharmacovigilance.

INTRODUCTION

Stevens–Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are severe mucocutaneous adverse reactions characterized by widespread keratinocyte apoptosis, epidermal necrosis, and epidermal detachment.[1,2] They are classified by body surface area (BSA) involvement as SJS (<10%), TEN (>30%), and SJS–TEN overlap (10%–30%) These conditions are medical emergencies associated with considerable morbidity and mortality, especially in older adults and patients with comorbidities.[1,3]

Medications are the most common triggers, with high-risk agents including sulfonamides, antiepileptics, allopurinol, nevirapine, and some antibiotics.[2,3,4] Although beta-lactam antibiotics are widely used, amoxicillin–clavulanic acid is a relatively uncommon cause of SJS/TEN.[4,5] We report a histopathologically confirmed case of SJS–TEN overlap in a 64-year-old man in whom amoxicillin–clavulanic acid was considered the most likely offending drug despite concomitant exposure to other medications.

CASE PRESENTATION

Patient Profile and Chief Complaints

A 64-year-old man weighing 52 kg presented to a tertiary care teaching hospital with widespread skin lesions, epidermal peeling, and painful oral erosions following recent drug exposure. He was a driver by occupation and had HIV infection diagnosed in 2015 on abacavir-based antiretroviral therapy, with a past history of treated pulmonary tuberculosis in 2016. Chronic tobacco chewing was documented. No previous similar cutaneous adverse reaction was reported.

Before admission, he had received oral amoxicillin–clavulanic acid 625 mg twice daily for 5–6 days for a febrile respiratory illness. He was also on antiretroviral therapy and had received HBsAg-related treatment/prophylaxis; exposure to acyclovir and unspecified ayurvedic medication was also noted in outside records. Despite concomitant medications, amoxicillin–clavulanic acid was considered the most likely offending drug based on the temporal relationship, improvement after withdrawal, and a probable Naranjo score of 6. Rechallenge was not performed.

Clinical Findings

On examination, he was hemodynamically stable. Cutaneous findings included multiple targetoid erythematous-to-dusky hyperpigmented macules, patches, and plaques over the face, neck, trunk, extremities, palms, and soles, with vesicobullous lesions, erosions, crusting, and epidermal peeling as shown in Figure 1a and 1b. Oral and genital mucosal involvement was present, and pseudo-Nikolsky sign was positive. Epidermal detachment involved approximately 25%–30% body surface area, consistent with SJS–TEN overlap.

Laboratory Findings

Investigations showed anemia (hemoglobin 8.4–8.7 g/dL), leukocyte count 3,600–9,500/mm^3, platelet count 238,000–405,000/mm^3, elevated C-reactive protein, hypoalbuminemia, and renal impairment with serum

creatinine up to 3.2 mg/dL, which later improved. Hyponatremia and mild hypokalemia were also noted. HIV serology was reactive, and CD4 count was 48 cells/µL (8%). Chest radiography showed left lung fibrocalcific changes, and ultrasonography revealed bilateral renal parenchymal disease.

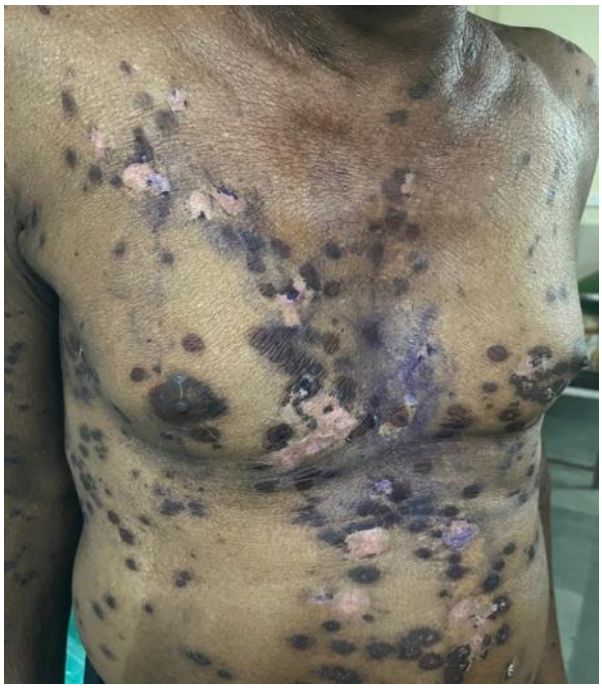

Figure 1a

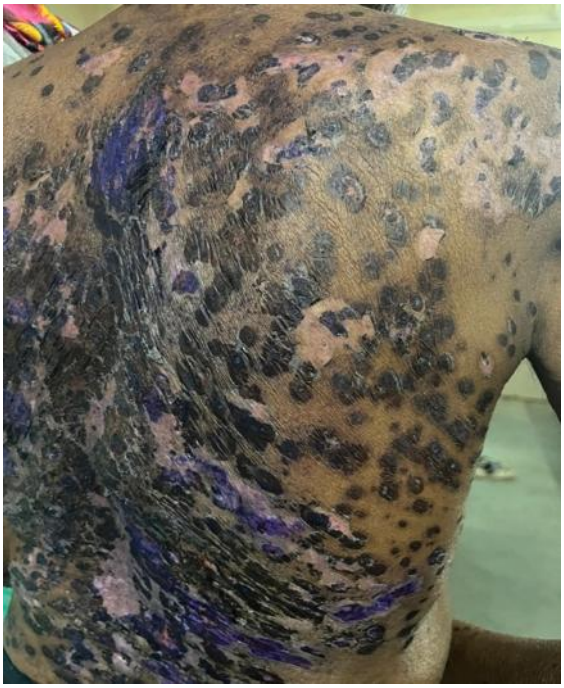

Figure 1b

Skin biopsy demonstrated epidermal ulceration and necrosis with basal vacuolization, dyskeratotic cells, and upper dermal lymphocytic infiltrate, consistent with toxic epidermal necrolysis. The final diagnosis was SJS–TEN overlap, with a SCORTEN of 2 and probable causality attributed to amoxicillin–clavulanic acid.

Management and Outcome

Amoxicillin–clavulanic acid was discontinued immediately, and other non-essential drugs were withheld. The patient received multidisciplinary care with supportive management including intravenous fluids, electrolyte correction, wound and mucosal care, pain control, and nutritional support. Systemic therapy included intravenous dexamethasone, intravenous immunoglobulin, and cyclosporine, along with topical treatment for erosions, antihistamines, proton pump inhibitor therapy, and vitamin/calcium supplementation.

During hospitalisation, active epidermal detachment subsided, erosions healed progressively, and oral intake improved. Serial investigations showed improvement in renal function and electrolyte abnormalities. Re-epithelialization of denuded areas with residual post-inflammatory hyperpigmentation and palmar desquamation occurred. No sepsis, respiratory failure, or hemodynamic instability was documented. The patient showed significant clinical recovery.

DISCUSSION

SJS and TEN are severe immune-mediated cutaneous adverse reactions caused by extensive keratinocyte apoptosis.[1,2] The biopsy findings in this case—epidermal necrosis, vacuolar degeneration, dyskeratotic cells, and mild dermal lymphocytic infiltrate—were consistent with this diagnosis.

Although the patient had exposure to multiple medications, amoxicillin–clavulanic acid was considered the most likely offending drug based on the close temporal relationship, improvement after withdrawal, and a probable Naranjo score of 6. This assessment is clinically important because HIV-positive patients are at increased risk of severe cutaneous adverse reactions due to immune dysregulation and polypharmacy.[4] The patient's marked immunosuppression, with a CD4 count of 48 cells/µL, may have increased this susceptibility.

Amoxicillin-associated SJS/TEN is rare but recognised.[3,5] Zaidi et al. reported amoxicillin and clavulanic acid-induced SJS, and our case extends the available evidence by documenting SJS–TEN overlap with histopathologic confirmation.[5] The diagnosis in this patient was supported by the characteristic mucocutaneous findings, positive pseudo-Nikolsky sign, biopsy consistent with TEN, and epidermal detachment involving 25%–30% BSA. A SCORTEN of 2 indicated clinically significant disease.[1]

Prompt withdrawal of the suspected drug and aggressive supportive care remain the mainstay of management.[1,2] In this case, supportive treatment combined with corticosteroids, intravenous immunoglobulin, and cyclosporine was associated with clinical recovery. This report also underscores the importance of pharmacovigilance reporting for rare but serious antibiotic-related adverse drug reactions.

CONCLUSION

Amoxicillin–clavulanic acid should be recognised as a rare but potentially life-threatening cause of SJS–TEN overlap. In this patient, despite concomitant exposure to other medications including abacavir-based therapy, the temporal profile and probable causality assessment favoured amoxicillin–clavulanic acid as the principal offending drug. Prompt withdrawal of the suspected agent, histopathologic confirmation, and aggressive supportive and immunomodulatory treatment resulted in recovery. This case reinforces the need for cautious antibiotic prescribing and robust pharmacovigilance in severe cutaneous adverse drug reactions.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent form. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understands that her name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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