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Successful Management of Etoricoxib-Induced Stevens-Johnson Syndrome/Toxic Epidermal Necrolysis with Corticosteroids: A Case Report

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KEYWORDS

Drug-induced hypersensitivity, Pharmacovigilance, Adverse drug reaction, Stevens-Johnson Syndrome, Toxic Epidermal Necrolysis

ABSTRACT:

Background: Stevens-Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN) are rare but life-threatening severe cutaneous adverse reactions characterized by widespread epidermal necrosis and detachment, often triggered by medications. Non-steroidal anti-inflammatory drugs (NSAIDs), including selective COX-2 inhibitors like etoricoxib, have been implicated in some cases.

Case Presentation: We report the case of a 59-year-old woman from Rajasthan with a known hypersensitivity to diclofenac who developed SJS following 22 days of etoricoxib therapy for a neck injury. She presented with dyspnoea, dysphagia, painful oral ulcers, erythematous skin lesions, widespread blisters and erosions, and a positive Nikolsky's sign. The patient was also noted to be malnourished upon examination.

Management: Etoricoxib was immediately discontinued. The patient received systemic antibiotics (piperacillin-tazobactam, clindamycin, doxycycline), corticosteroids (dexamethasone), and supportive care, including fluid and electrolyte replacement, protein supplementation, wound care, and topical treatments. Intravenous immunoglobulins and cyclosporine were not administered due to financial limitations.

Outcome: The patient's condition gradually improved with systemic corticosteroids and supportive measures. She was discharged in a stable state, although some ophthalmic complications persisted.

Conclusion: This case highlights a rare instance of etoricoxib-induced SJS in India. It emphasizes the critical role of clinical judgment in diagnosing and managing drug-induced SJS/TEN, the potential risks associated with NSAIDs, and the importance of vigilant pharmacovigilance and post-marketing drug surveillance to safeguard patient health.

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1. Introduction

Stevens-Johnson Syndrome (SJS) is a rare but serious adverse reaction involving the skin and mucous membranes, often triggered by medications, infections, genetic predisposition (HLA-B*1502 gene), autoimmune diseases, liver diseases, or diabetes. It initially presents with flu-like symptoms, progressing to widespread skin redness, blisters, and mucosal erosions, frequently affecting the oral mucosa, genital mucosa (balanitis, colpitis), and ocular surfaces (severe conjunctivitis, blepharitis) [1, 4]. Toxic Epidermal Necrolysis (TEN) is a more severe form of SJS, characterized by skin detachment involving more than 30% of the body surface area (BSA) [1]. SJS is a type IV hypersensitivity reaction, where cytotoxic T cells and natural killer cells release signals like fas/fas ligand and perforin/granzyme B in response to the causative drug or their byproducts, causing keratinocyte apoptosis and skin detachment [2,3].

Etoricoxib, a selective COX-2 inhibitor used for osteoarthritis, rheumatoid arthritis, and gout, has been linked to SJS, typically developing within 20–50 days of exposure [4, 5]. In India, the incidence of SJS/TEN within Cutaneous Adverse Drug Reactions (CADRs) is 6.84%, with a mortality rate reaching up to 50% [6, 7].

2. Case Presentation

Chief Complaints:

A 59-year-old woman was brought to the emergency department of a tertiary care hospital in Rajasthan with chief complaints of dyspnoea (RR = 24), dysphagia, multiple oral ulcers, photophobia, and multiple erythematous to violaceous pea-sized skin lesions spread across her body. She had experienced a hypersensitivity reaction two years ago after taking Diclofenac sodium 75 mg twice daily for three days.

Past Medication History:

The patient sustained a neck injury 23 days prior and was prescribed Etoricoxib, Pregaba M, and a combination of Aceclofenac, Paracetamol, and Chlorzoxazone. After 22 days of treatment, she developed multiple oral ulcers and photophobia, followed by pinpoint erythematous lesions starting on the upper limbs and spreading to the rest of the body, evolving into blisters. She also developed a fever and was initially treated with IV fluids at a hospital nearby. As the patient's condition worsened, family members transferred her to a tertiary care hospital for specialized care.

Clinical examination:

The Dermatology team found the patient as malnourished, with multiple erythematous to violaceous blisters and erosions (0.3×0.3 mm to 5×5 cm in size) on the limbs, trunk, back, face, palms, and soles. Oral ulcers, drooling of white fluid, a positive Nikolsky's sign, and conjunctival involvement with lesions, excoriations, epidermal peeling, and white discharge were seen. ENT evaluation revealed extensive bullous lesions in the oral and nasal mucosa, with ruptured bleeding erosions. Pan-mucosal involvement caused severe pain during swallowing, nasal obstruction, crusting, and epistaxis. ECG showed sinus bradycardia, and a Braden Scale assessment indicated high pressure ulcer risk. Due to financial constraints, the patient declined a Drug Allergy Test and Skin Biopsy. Based on clinical judgment and circumstantial evidence, a diagnosis of Stevens-Johnson Syndrome-Toxic Epidermal Necrolysis (SJS-TEN) overlap was made.

SCORTEN score:

The patient's SCORTEN score was calculated to be 3 (Table 1), which predicts a mortality rate of 35.3%. [8]

3. Treatment:

Upon admission, Tab Etoricoxib was immediately withdrawn, and patient was admitted to ICU, where she received injection Piperacillin-Tazobactam 4.5 g 8 hourly, Injection Clindamycin 600 mg 12 hourly, and Injection Doxycycline 100 mg 12 hourly, along with Betadine and Candida gargles for oral ulcers. Adequate fluid replacement along with protein powder supplementation by RT feed was done. Oral Metaproterenol 10 mg was advised for dyspnoea, and BP was optimized with Tab Telmisartan 40 mg 12 hourly, Tab Amlodipine 5 mg 24 hourly & Nitro-glycerine infusion (titrated from 5 – 20 mcg/ min). For eye lesions, Ointment Moxifloxacin 0.5% and Sodium hourly Carboxymethylcellulose gel were prescribed. Tablet Fexofenadine 120 mg, Fusidic acid cream, and liquid paraffin were also added for lesions. By the fourth day, Inj. Dexamethasone 4 mg q 8 hourly daily was started. Broad spectrum Antifungal cover was given with Tab Fluconazole 50mg 24 hourly daily. Lesions began

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drying, and no fresh eruptions were observed. On the sixth day, Metaproterenol was discontinued. Inj. Dexamethasone was tapered to 4 mg 12 hourly daily, and the same treatment was continued. By eighth day, Dexamethasone 4 mg was switched to Tab Prednisolone 60 mg 24 hourly daily, tab Fluconazole was reduced to once weekly, and tablet Methylcobalamin with Folic acid 5 mg was added. Upon discharge, the patient was prescribed Levocetirizine 5mg daily, Ketoconazole 0.1% oral paste, Clobetasol, and Fusidic acid cream.

PARAMETER	SCORE RANGE	VALUE	SCORE
Age (in years)	>40	59	1
Malignancy	NONE	-	0
Body surface area (in percent)	>10	30	1
Heart rate (beats per minute)	>120	51 bpm	0
Serum bicarbonate (mmol/l)	<20	18.4 mmol/L	1
Serum glucose (mmol/l)	>14	8.3 mmol/L	0
Serum urea (mmol/l)	>10	1.8 mmol/L	0

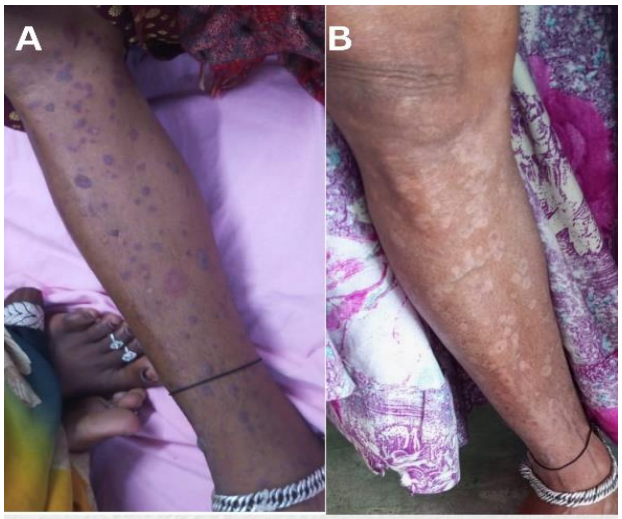

FIGURE 1:
A. Picture shows numerous erythematous, pinpoint-sized violaceous lesions at the skin surface
B. Picture shows left limb after 3 weeks of treatment. Lesions can be seen receding.

4. Prognosis:

Patient was discharged after nine days of treatment with stable vitals. Upon discharge, new lesions were not observed. Old blisters and lesions had also healed.

5. Discussion:

SJS-TEN overlap is a rare, potentially life-threatening mucocutaneous reaction affecting 10–30% of the body surface area, [1] marked by epidermal detachment, mucosal erosions, and serious systemic symptoms. No other inciting agents were identified during clinical examinations, and the patient had no significant toxin exposure or relevant family history. Hypersensitivity reaction to diclofenac sodium (a COX-2 inhibitor NSAID) 2 years ago suggests the current instance of SJS/TEN was drug-induced. NSAIDs, commonly prescribed worldwide, are a leading cause of adverse drug reactions. [9] Etoricoxib, a selective COX-2 inhibitor, is widely used for managing chronic inflammatory pain. [5] Aceclofenac, another NSAID in the same class, also has significant anti-inflammatory and analgesic effects. [10] These drugs trigger the immune system, activating cytotoxic T lymphocytes and MHC-1. As these drugs are too small to induce an

FIGURE 2:
A. Picture depicts ulceration on lower lip and developing lesions under eyes.
B. Picture taken 3 weeks after treatment.Ulcers and lesions have receded.

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immunogenic response, three models—Hapten/ Pro hapten Concept, Pie Model, and Altered repertoire Model— have been proposed to explain MHC-1 activation. [9] Skin biopsy and Drug Allergy Test are standard diagnostic procedures for confirming SJS/TEN and identifying the causative drug, [1] but the patient was unable to undergo these procedures due to financial constraints. While it was clear that the patient had been exposed to both potentially causative drugs, the duration between exposure to drug and occurrence of first symptoms (23 Days in this case) is strongly suggestive of Etoricoxib being the causative agent, as multiple cases of Aceclofenac-induced SJS have reported the onset of symptoms within a week of drug exposure. [10,11]

The management of SJS-TEN overlap includes systemic steroids to block cytotoxic T cells and macrophages. Intravenous immunoglobulins (IV-Ig) inhibit Fas-mediated keratinocyte death and granzyme B release, halting disease progression. Various pharmacological agents, including IV-Ig with or without steroids, cyclosporine, systemic corticosteroids, and Etanercept, are used. [1] Due to financial constraints, the patient received intravenous dexamethasone (a corticosteroid) and supportive care (antibiotics, IV fluids), leading to gradual stabilization without IV-Ig and cyclosporine. The patient achieved an almost complete recovery with the use of corticosteroids alone, except for certain ophthalmic issues, which are in line with the known long-term effects of SJS for which she is still under ophthalmological treatment.

6. Conclusion:

This case from Rajasthan, India, links Etoricoxib to Stevens-Johnson Syndrome (SJS) and highlights successful treatment without cyclosporine or IVIG, using basic supportive care. It underscores the role of clinical judgment and prompt intervention and highlights the risk of severe adverse reactions from widely available NSAIDs. The case stresses the need for prompt documentation and post-marketing surveillance to improve patient safety and guide clinical decisions.

7. Acknowledgement:

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8. Conflict of interest:

The authors declare no conflict of interest about the publication of this research.

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