International Journal of Zoology, Environment And Life Sciences

Content Available at www.lapinjournals.com ISSN (O): 3048-9598

Case Study Open Access

REVEALING THE RISKS: STEVENS - JOHNSON SYNDROME INDUCED BY DICLOFENAC- FROM PAIN RELIEF TO DERMATOLOGICAL CRISIS

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Article History: Received: 21 June 2024, Revised: 11 July 2024, Accepted: 02 Aug 2024, Published: 15 Aug 2024

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DOI: https://doi.org/10.70604/ijzels.v1i1.2

Abstract:

Stevens-Johnson Syndrome (SJS) is a rare but potentially fatal skin reaction to medications, frequently triggered by drugs like nonsteroidal anti-inflammatory drugs (NSAIDs), including diclofenac. This case describes a 39-year-old male who developed erythematous lesions and exfoliative dermatitis five days after receiving Diclofenac. The patient exhibited characteristic symptoms of SJS, including widespread skin fragility and a positive indirect Nikolsky sign. Prompt management involved discontinuation of Diclofenac, administration of corticosteroids (Dexamethasone), and immunosuppressants like Cyclosporine to suppress the immune response. Antibiotics (Linezolid and Azithromycin) were used to prevent secondary infections, while topical agents (Miconazole, Betamethasone) addressed skin lesions and fungal colonization. Pharmacists played a key role in this multidisciplinary approach by reviewing the patient's medication history, recommending alternatives to high-risk drugs, and providing education on early signs of adverse drug reactions. Additionally, they monitored immunosuppressant dosing to minimize nephrotoxicity and ensured proper use of topical treatments. Post-discharge follow-up focused on preventing long-term complications such as scarring and chronic mucosal damage. This case underscores the vital contributions of pharmacists in managing drug-induced SJS through vigilant monitoring, patient education, and optimizing pharmacological interventions.

Keywords: Stevens-Johnson Syndrome, Diclofenac, NSAIDs, drug reaction, immune modulation, pharmacist interventions, Cyclosporine, corticosteroids.

Introduction

Stevens-Johnson Syndrome (SJS) is a serious skin reaction marked by extensive skin detachment, involvement of mucous membranes, and systemic symptoms. This life-threatening condition is often triggered by specific medications, including antibiotics, anticonvulsants, and nonsteroidal anti-inflammatory drugs (NSAIDs) [1]. Among NSAIDs, Diclofenac is one of the commonly implicated agents, known for its efficacy in managing pain and inflammation but also associated with rare, yet serious, hypersensitivity reactions such as SJS [2].

The pathophysiology of Diclofenac-induced SJS involves an immune-mediated mechanism that leads to apoptosis of keratinocytes, primarily triggered by cytotoxic T-cells and the release of pro-inflammatory cytokines [3]. Genetic predispositions, such as specific HLA types, are considered significant factors in the susceptibility to drug-induced SJS, but the precise mechanism remains complex and multifactorial. Clinically, SJS presents with flu-like symptoms followed by rapid onset of painful erythematous or purpuric macules that coalesce, leading to epidermal detachment. Early recognition and discontinuation of the offending drug are critical in managing SJS, as delayed diagnosis and treatment can result in significant morbidity and mortality. The mortality rate for SJS ranges from 1% to 5%, underscoring the importance of prompt intervention [4].

Although the therapeutic use of Diclofenac is widespread due to its anti-inflammatory properties, its potential to cause life-threatening adverse effects like SJS highlights the need for cautious use,

particularly in patients with a history of drug allergies or other risk factors. Given the severity of the condition, understanding the clinical presentation and risk factors associated with Diclofenac-induced SJS is crucial for clinicians to mitigate risks and improve patient outcomes [5].

Case Study

A 39-year-old male, was admitted to the Dermatology Ward with erythematous lesions and scarring on the face, upper trunk, back, and lower limbs for 5 days. He was asymptomatic until 3 days prior when the lesions appeared. Ten days ago, he received an intramuscular injection of Diclofenac for fever and body pains, and the skin lesions developed 5 days later. His medical history is notable for a stroke 2 months ago; he is non-diabetic and non-hypertensive. He has been consuming alcohol and smoking for 20 years.

On examination, he had diffuse exfoliative dermatitis-like lesions with scaling over the face, upper and lower limbs, and trunk, along with diffuse erythema, crusted lesions in the axillary folds, nape of the neck, and retroauricular area. There were multiple erythematous erosions with oozing on the back, scrotum, and neck. Tinea cruris lesions were present, but the buccal, genital, anal, and eye mucosa were normal. He also exhibited burning and cuts on the lips with cheilitis. Nikolsky's sign was negative on direct testing but positive on indirect testing. Investigations revealed cholelithiasis on ultrasound abdomen, with a complete blood picture showing hemoglobin of 14 g/dL, platelet count of 4,50,000 cells/cumm, WBC count of 15,000 cells/cumm, eosinophils at 4%, and lymphocytes at 33%. Liver function tests showed total bilirubin of 1.3 mg/dL, indirect bilirubin of 1 mg/dL, direct bilirubin of 0.3 mg/dL, ALP of 129 IU/dL, SGOT of 30 IU/dL, and SGPT of 69 IU/dL. Viral markers (HbsAg, HCV, and HIV) were all non-reactive. Vital signs were stable throughout the hospital stay, with BP ranging from 120/80 mmHg to 130/80 mmHg, pulse rate between 80-94 bpm, and consistently afebrile with SpO2 levels at 97-98%.

Based on the clinical presentation and investigation findings, the patient was diagnosed with a cutaneous drug reaction, specifically Stevens-Johnson Syndrome (SJS), likely caused by Diclofenac. The medications administered included Pantoprazole, Pheniramine Maleate, Linezolid, Dexamethasone, Azithromycin, Fluconazole, Cyclosporine, Miconazole cream, Fucidic acid with Betamethasone, and normal saline. Upon discharge, the patient was prescribed Pantoprazole 40 mg OD, Niacinamide BD, Fluconazole 200 mg twice a week, Linezolid 600 mg BD, Miconazole cream 2% BD for topical application, and Betamethasone 1% ointment OD for topical application. He was advised to follow up in the outpatient department after 15 days for further evaluation.

Discussion

The described case highlights Stevens-Johnson Syndrome (SJS), a rare but severe cutaneous adverse reaction, often induced by medications such as nonsteroidal anti-inflammatory drugs (NSAIDs) like Diclofenac [3, 6]. SJS presents with widespread erythematous lesions, skin exfoliation, and mucocutaneous involvement. The timeline of this patient's symptom onset-5 days after Diclofenac administration-aligns with drug-induced SJS patterns, wherein symptoms typically manifest within 1 to 3 weeks following drug exposure [7].

Diclofenac has been implicated in drug hypersensitivity reactions, including SJS, with the pathogenesis linked to an immune-mediated process involving keratinocyte apoptosis, typically driven by cytotoxic T-cells and Fas ligand interactions. The positive indirect Nikolsky sign in this patient reflects the skin's fragility, a hallmark of SJS [8].

Management of SJS involves the prompt discontinuation of the offending drug and supportive care, as was done in this case. The administration of corticosteroids (Dexamethasone) and immunosuppressants like Cyclosporine has been employed to modulate the immune response and reduce inflammation. The use of Cyclosporine in SJS has been supported by literature for its ability to inhibit T-cell activation and reduce mortality. However, its use remains controversial, with concerns over potential nephrotoxicity, which requires close monitoring during treatment [9].

The patient was also treated with antibiotics (Linezolid and Azithromycin) to prevent or treat secondary infections, which are common in patients with extensive skin barrier disruption. Topical treatments such as Miconazole and Betamethasone are used to manage skin lesions and control fungal colonization or infections like Tinea cruris, as seen in this patient [10, 11, and 12].

Follow-up after discharge is crucial for SJS patients, as they remain at risk for long-term complications such as scarring, pigmentary changes, and, in more severe cases, chronic mucosal damage. Monitoring

and managing post-inflammatory sequelae are essential aspects of long-term care.

Conclusion

In conclusion, Stevens - Johnson syndrome (SJS) is a life-threatening dermatological emergency that requires prompt identification and immediate cessation of the offending agent, in this case, Diclofenac. The comprehensive management of SJS revolves around supportive care, immune modulation, and infection prevention. Pharmacists play a vital role in this multidisciplinary approach by ensuring accurate drug selection, monitoring for adverse effects, and counseling on medication compliance and potential triggers. In this case, pharmacist interventions could have focused on reviewing the patient's medication history to identify high-risk drugs, educating the patient on early signs of adverse drug reactions, and recommending alternatives to high-risk NSAIDs like Diclofenac.

Additionally, pharmacists can assist in adjusting doses of immunosuppressants like Cyclosporine to balance efficacy and minimize nephrotoxicity. Close monitoring of antibiotics like Linezolid and Azithromycin is essential to prevent secondary infections, a common complication in SJS patients. Furthermore, pharmacists can counsel on proper use of topical treatments such as Miconazole and Betamethasone for managing skin lesions and preventing fungal infections. Lastly, the pharmacist's role extends beyond the acute phase by ensuring follow-up care, monitoring for long-term complications, and promoting adherence to prescribed medications to prevent relapse or complications. In summary, through vigilant monitoring and timely interventions, pharmacists can significantly improve patient outcomes in the management of drug-induced SJS.

Conflict of Interest

The authors declare that there are no conflicts of interest.

Acknowledgement

Author is thankful to the Superintend and Head of the department, of Dermatology in Government General Hospital, Guntur.

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