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ETORICOXIB-INDUCED ERYTHEMA MULTIFORME-LIKE DRUG ERUPTION: A CASE REPORT

Pharmacology

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ABSTRACT

Etoricoxib is a selective cyclo-oxygenase-2 (COX-2) inhibitor commonly used for the management of pain and inflammatory conditions because of its better gastrointestinal tolerability compared with non-selective nonsteroidal anti-inflammatory drugs (NSAIDs). Although generally well tolerated, rare cutaneous adverse drug reactions have been reported. We report the case of a 46-year-old woman with arthritis who developed pruritic, scaly, erythematous targetoid lesions over both hands, lower limbs, feet, and the nape of the neck after receiving etoricoxib along with other medications for knee and generalized body pain. Clinical findings were suggestive of an erythema multiforme-like drug eruption. Based on the temporal relationship and improvement following drug withdrawal, etoricoxib was considered the suspected offending agent. Causality assessment showed a possible association with etoricoxib (Naranjo score: 4; WHO-UMC scale: possible). The reaction was graded as moderate according to the Hartwig severity scale and was considered not preventable by the modified Schumock and Thornton criteria. The drug was discontinued, and the patient was managed conservatively, resulting in significant clinical improvement. Rechallenge was not performed because of the risk of recurrence. This case highlights the importance of early recognition and prompt withdrawal of etoricoxib in suspected cutaneous adverse drug reactions.

KEYWORDS

Adverse Drug Reaction; Etoricoxib; Erythema Multiforme-like Drug Eruption; Cox-2 Inhibitor

INTRODUCTION

Erythema multiforme (EM) is an acute, immune-mediated mucocutaneous disorder characterized by fixed targetoid or atypical target lesions distributed symmetrically over the extremities, particularly the acral surfaces. It is most commonly associated with infections, especially herpes simplex virus and *Mycoplasma pneumoniae*, whereas drug-induced cases are less frequent but clinically significant. Among medications, non-steroidal anti-inflammatory drugs (NSAIDs) are recognized but uncommon triggers [1].

Etoricoxib is a selective cyclo-oxygenase-2 (COX-2) inhibitor widely used for the management of pain and inflammatory conditions because of its favorable gastrointestinal safety profile. Although generally well tolerated, rare cutaneous adverse drug reactions have been reported with etoricoxib, including urticaria, fixed drug eruption, Stevens–Johnson syndrome, toxic epidermal necrolysis, and erythema multiforme-like eruptions [2].

Because such reactions are uncommon and potentially under-recognized, reporting individual cases remains important for pharmacovigilance and early recognition of serious cutaneous adverse reactions. We report a suspected case of etoricoxib-induced erythema multiforme-like drug eruption in a 46-year-old woman.

Case Presentation

A 46-year-old woman presented to the Dermatology outpatient department with complaints of multiple pruritic, scaly skin lesions over both upper and lower limbs, including the hands and feet. She was a known case of arthritis and had been receiving treatment for knee and generalized body pain at another hospital. During this period, she had received multiple medications, including etoricoxib 90 mg, which was identified as the suspected offending drug.

The lesions appeared 2 days after initiation of etoricoxib. Initially, the lesions developed over the hands and gradually progressed in number and distribution. Cutaneous examination revealed multiple erythematous, scaly targetoid lesions involving the hands, forearms, lower limbs, feet, and nape of the neck (Figure 1).

Figure 1. Clinical photographs at initial presentation demonstrating erythematous, scaly lesions involving the dorsal and palmar aspects of the hands, feet, and ankles.

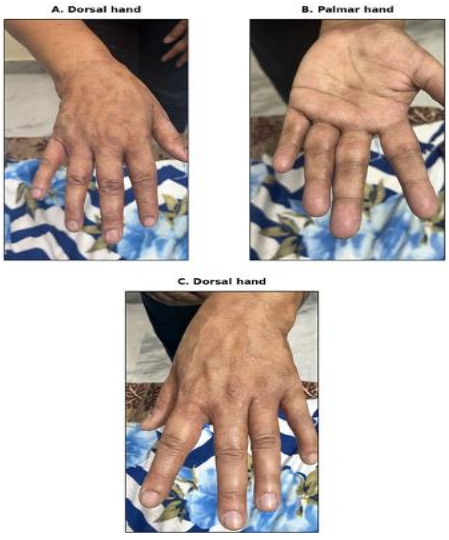
There was no history of recurrent herpes infection, oral or genital lesions, fever, or prodromal symptoms suggestive of active herpes simplex virus infection.

Based on the temporal association, clinical morphology, and drug history, a provisional diagnosis of erythema multiforme-like drug eruption secondary to etoricoxib was made.

Laboratory investigations revealed positivity for herpes simplex virus (HSV-1/2), elevated erythrocyte sedimentation rate (ESR), and evidence of urinary tract infection.

Etoricoxib was discontinued, and the patient was managed conservatively with symptomatic treatment. Clinical improvement was observed within 3 days of drug withdrawal, with reduction in erythema, scaling, and pruritus. The patient was discharged in stable condition. Follow-up examination showed marked resolution of lesions with residual post-inflammatory pigmentation (Figure 2).

Figure 2. Follow-up photographs showing marked improvement of the dorsal and palmar aspects of the hands, with residual post-inflammatory pigmentation.



Causality assessment using the Naranjo Adverse Drug Reaction Probability Scale yielded a score of 4, indicating a possible association. The reaction was also categorized as "possible" according to the World Health Organization–Uppsala Monitoring Centre (WHO-UMC) scale. A definite causal relationship could not be established because of concomitant medications, documented HSV positivity (a known trigger for erythema multiforme), and the absence of drug rechallenge. Rechallenge was not attempted because of ethical concerns and the risk of recurrence.

DISCUSSION

This case describes a suspected erythema multiforme (EM)-like drug eruption temporally associated with etoricoxib exposure in a 46-year-old woman. The lesions predominantly involved acral sites, including the hands, feet, and lower limbs, and showed significant improvement following withdrawal of the suspected drug and conservative management.

EM is an acute immune-mediated mucocutaneous disorder most commonly associated with infections, particularly herpes simplex virus (HSV), whereas drug-induced EM is relatively uncommon [1]. Among medications, non-steroidal anti-inflammatory drugs (NSAIDs) are recognized but infrequent triggers [1]. Although etoricoxib is generally considered well tolerated because of its selective cyclo-oxygenase-2 (COX-2) inhibition and improved gastrointestinal safety profile, rare cutaneous adverse reactions including fixed drug eruption, Stevens–Johnson syndrome, toxic epidermal necrolysis, and EM-like eruptions have been documented [2].

A similar case was reported by Thirion et al. in 2008, describing an etoricoxib-induced EM-like eruption in a 69-year-old man receiving etoricoxib 90 mg/day [2]. The present case differs with respect to patient demographics and lesion distribution, but further supports the possibility of etoricoxib-associated EM-like reactions.

The exact mechanism underlying etoricoxib-induced erythema multiforme-like eruptions remains unclear. Drug-induced EM is believed to involve a cell-mediated hypersensitivity reaction resulting in keratinocyte injury and inflammation. Similar immunological mechanisms have been proposed for other NSAID-associated cutaneous adverse reactions. Although selective COX-2 inhibitors are generally associated with improved gastrointestinal tolerability, clinicians should remain vigilant for rare but potentially serious mucocutaneous adverse reactions [2].

Causality assessment in this case was challenging because the patient had received multiple concomitant medications, including other NSAIDs and supportive drugs, which could potentially contribute to cutaneous eruptions. In addition, HSV-1/2 seropositivity was detected. However, HSV IgG positivity generally reflects prior exposure rather than active infection. Furthermore, the absence of recurrent herpes infection, oral or genital lesions, fever, and prodromal symptoms reduced the likelihood of active HSV-triggered EM. The close temporal relationship between etoricoxib exposure and onset of lesions, along with clinical improvement after drug withdrawal, supported a possible association with etoricoxib.

The Naranjo Adverse Drug Reaction Probability Scale yielded a score of 4, indicating a possible association with etoricoxib [3]. The reaction was also categorized as "possible" according to the World Health Organization–Uppsala Monitoring Centre (WHO-UMC) causality criteria [4]. Rechallenge was not attempted because of ethical concerns and the potential risk of recurrence.

Severity assessment using the Hartwig severity scale categorized the reaction as moderate (Level 3), as withdrawal of the suspected drug and symptomatic treatment were required, without intensive care admission, permanent disability, or mortality [5]. Preventability assessment using the modified Schumock and Thornton criteria suggested that the reaction was not preventable, as no prior history of etoricoxib hypersensitivity, medication error, inappropriate dosing, or clearly avoidable risk factor was identified [6].

Skin biopsy was not performed, which represents a limitation of this report. Additionally, concomitant medications and HSV seropositivity limited definitive attribution of causality. Nevertheless, the clinical presentation, temporal association, and improvement following drug withdrawal support the likelihood of an etoricoxib-associated EM-like eruption.

This case highlights the importance of obtaining a detailed medication history, recognizing uncommon cutaneous adverse drug reactions, and promptly discontinuing the suspected offending agent. Clinicians should remain aware that even selective COX-2 inhibitors may rarely cause clinically significant mucocutaneous reactions requiring early identification and management.

CONCLUSION

This case suggests a possible association between etoricoxib and an erythema multiforme-like drug eruption in a 46-year-old woman. Although concomitant medications and HSV seropositivity represented important confounding factors, the temporal relationship and clinical improvement following withdrawal of etoricoxib support its role as a suspected trigger. Early recognition, prompt discontinuation of the offending drug, and supportive management are essential to prevent progression and recurrence of cutaneous adverse drug reactions.

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