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Fixed drug eruption induced by Etoricoxib in Thailand: A case report

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ABSTRACT

Etoricoxib, a commonly prescribed non-steroidal anti-inflammatory drug (NSAID), has been associated with adverse cutaneous reactions, including fixed drug eruption (FDE). We describe a case report of a 37-year-old Thai male who developed erythematous plaques and bullous lesions following the ingestion of a 90 mg dose of Etoricoxib. The lesions were located on the lateral aspect of the right leg near the popliteal fossa, the dorsal aspect of the right foot, the medial aspect of the right arm, and the left lumbar region. Symptoms began two hours post-ingestion with pruritus, progressing to erythema and bullous formation over the subsequent 72 h. The patient was treated with oral Prednisolone, antihistamines, and topical steroids, resulting in significant clinical improvement within 12 days. This case highlights the potential of Etoricoxib to trigger generalized bullous fixed drug eruption (GBFDE), which is a more severe variant involving more than three body sites and classified as one of the Severe Cutaneous Adverse Reactions (SCARs), emphasizing the need for prompt recognition and appropriate management to prevent recurrence and mitigate symptoms.

1. Introduction

Adverse drug reactions are a significant concern in clinical practice, with cutaneous manifestations being among the most common presentations. These reactions can range from mild rashes to severe and life-threatening conditions [1]. Fixed Drug Eruption (FDE) is a well-recognized form of drug allergy that manifests as recurrent, well-demarcated erythematous plaques or patches at the same anatomical site upon re-exposure to the offending drug [2–4]. FDE can present in different forms, ranging from localized lesions to more severe variants. Generalized Bullous Fixed Drug Eruption (GBFDE) is a severe variant involving multiple anatomical sites, classified as a Severe Cutaneous Adverse Reaction (SCAR) due to its significant risk of complications [5]. Commonly implicated medications include non-steroidal anti-inflammatory drugs (NSAIDs), antibiotics, and anticonvulsants [6–8]. Among NSAIDs, selective cyclooxygenase-2 (COX-2) inhibitors, such as Etoricoxib, have been increasingly reported as triggers of FDE [3,9,10].

Etoricoxib is widely used for its anti-inflammatory and analgesic properties, particularly in managing chronic conditions like osteoarthritis and rheumatoid arthritis. While its selective inhibition of the COX-2 enzyme offers an improved gastrointestinal safety profile compared to traditional NSAIDs, its role in triggering FDE is a growing concern [9–11]. With the expanding use of COX-2 inhibitors, it is important for clinicians to be aware of their potential to cause adverse reactions, such as FDE, and to promptly recognize and manage such reactions to prevent recurrence.

2. Case report

A 37-year-old Thai male with no prior drug allergies presented with erythematous, pruritic plaques over his lateral aspect of the right leg, near the popliteal fossa, the dorsal aspect of the right foot, the medial aspect of the right arm and the left lumbar region, which developed

Abbreviations: FDE, Fixed drug eruption; NSAID, non-steroidal anti-inflammatory drug.

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Table 1
Symptom progression timeline.

Time Since Etoricoxib ingestion	Symptom Progression
0 h	Etoricoxib 90 mg ingested
2 h	Pruritus begins
5 h	Erythema intensifies
24–48 h	Bullous lesions develop
72	Bullous lesions rupture

approximately two hours after ingesting a 90 mg dose of Etoricoxib for acute muscle pain due to heavy lifting. The patient reported that the initial symptoms of mild pruritus began around 12:00 p.m., and by the afternoon, the erythema had intensified. Within the following 24–48 h, the plaques evolved into bullous lesions that ruptured around 72 h after onset (Table 1). On physical examination, the patient exhibited multiple, well-defined erythematous plaques on the back, upper and lower limbs, with particularly large lesions on the right dorsum of the foot and the back (Fig. 1). The patient had no fever or systemic symptoms. A detailed medical history revealed a similar, but less severe, episode on the back that had previously gone undiagnosed. Based on clinical findings, the diagnosis of generalized bullous fixed drug eruption (GBFDE) was made by a dermatologist, differentiating it from Stevens-Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN). Complete blood count and biochemical investigations were unremarkable. The patient was advised to discontinue Etoricoxib and treated with a five-day course of oral Prednisolone, antihistamines, and topical corticosteroids. Significant improvement was noted within 12 days, with complete resolution of some lesions. At the one-month follow-up, the patient exhibited complete healing with residual hyperpigmentation. He was counseled to avoid COX-2 inhibitors like Etoricoxib and provided with an allergy identification card.

3. Discussion

FDE is a distinctive cutaneous drug reaction, typically characterized by the reappearance of lesions in the same location upon repeated exposure to the causative drug [12,13]. GBFDE represents a more severe variant, involving multiple body sites (>3) and greater skin surface area, often mimicking conditions like SJS or TEN. GBFDE, however, tends to have a more favorable prognosis and less severe oral involvement compared to SJS/TEN. Differentiation between GBFDE and SJS/TEN can often be made via skin biopsy, which may show a characteristic interface dermatitis and prominent eosinophilic infiltration in GBFDE compared to the extensive epidermal necrosis seen in SJS/TEN [5,14].

The pathophysiology of FDE involves a type IV hypersensitivity reaction, specifically a delayed-type response [12,15]. Upon initial exposure to the drug, the drug or its metabolite binds to basal keratinocytes in the skin, which present the antigen to CD8+ T-cells. These CD8+ T-cells, specific to the drug antigen, persist in the epidermis as resident memory T-cells. Upon re-exposure to the drug, these memory T-cells are reactivated, releasing pro-inflammatory cytokines such as interferon-gamma (IFN-γ) and tumor necrosis factor-alpha (TNF-α) [12,15,16]. This cytokine release triggers localized inflammation and tissue damage, resulting in the characteristic erythematous and sometimes bullous lesions of FDE [13,17].

Etoricoxib, a COX-2 selective inhibitor, has gained attention for its role in FDE due to its widespread use and emerging case reports of such reactions [3,9,10,18]. While traditional NSAIDs are well-documented triggers of FDE, COX-2 inhibitors like Etoricoxib are increasingly recognized as potential culprits [9,19]. This recognition is crucial because COX-2 inhibitors are often prescribed to patients who may not tolerate other NSAIDs due to gastrointestinal concerns, yet these patients may still be at risk for cutaneous adverse reactions [19,20]. The differentiation between COX-1 and COX-2 inhibitors is important in managing cases like this because while COX-2 inhibitors such as Etoricoxib can induce FDE, patients may still tolerate COX-1 inhibitors without recurrence.

In addition to NSAIDs, other classes of drugs frequently associated with FDE include antibiotics such as cotrimoxazole, tetracyclines, and quinolones, as well as anticonvulsants and antimalarials [6,7]. The clinical management of FDE centers on the immediate cessation of the offending drug, which leads to the resolution of lesions within days to weeks [4,6]. Supportive therapies, such as topical corticosteroids and oral antihistamines, are commonly employed to reduce symptoms such as itching and inflammation [2,13]. In the case of GBFDE, management parallels that of SJS/TEN, with a focus on discontinuing the offending drug, providing supportive care, and managing complications. The prognosis of GBFDE remains favorable compared to SJS/TEN, particularly in the absence of severe mucosal involvement or systemic symptoms [5]. Confirming the causative drug may involve performing an oral challenge test, which is considered the gold standard for diagnosing drug allergies. However, it is recommended only under controlled conditions, especially in cases where more than three lesions are involved or there is oral mucosal involvement [5].

Preventing recurrence is a key aspect of managing FDE and GBFDE, as re-exposure to the same or structurally related drugs can result in more severe lesions and prolonged recovery [2,5]. Patient education is critical, as patients must be informed of the risk of recurrence and the

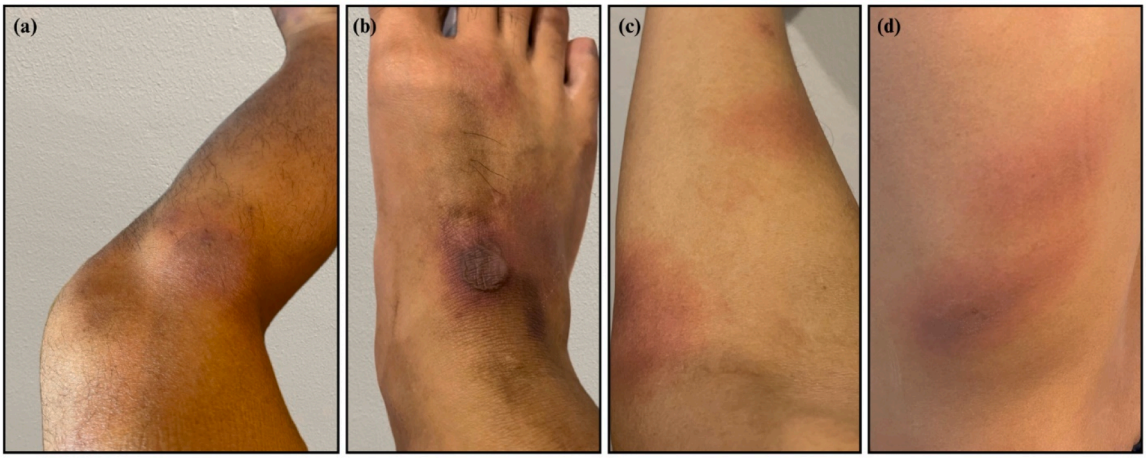

Fig. 1. Well-demarcated erythematous patches with a dusky violaceous hue and central darkening, consistent with the characteristics of fixed drug eruption. (a) On the lateral aspect of the right leg, near the popliteal fossa. (b) On the dorsal aspect of the right foot. (c) On the medial aspect of the right arm. (d) On the left lumbar region.

need to avoid the causative drug [21]. Cross-reactivity between structurally similar drugs should also be considered, and alternative therapies should be discussed with patients [2,22]. For drugs like Etoricoxib, the growing body of case reports underscores the importance of vigilance when prescribing to patients with a known history of drug allergies or adverse reactions [3,9,18,19]. Therefore, caution should be exercised when using these medications, and they should only be used according to the recommendations of a physician or pharmacist.

4. Conclusions

This case underscores the potential for Etoricoxib to induce FDE and highlights the importance of prompt recognition and management. FDE should be considered in patients with a history of erythematous plaques upon drug exposure, especially when associated with NSAIDs. Early discontinuation of the causative drug, along with supportive therapy, can lead to resolution of symptoms. Clinicians should educate patients on avoiding similar drugs to reduce the risk of recurrence, as recurrent FDE lesions can result in long-term pigmentary changes.

CRediT authorship contribution statement

Metar Siriwattanasatorn: Supervision, Conceptualization. **Pratya Phetkate:** Writing – review & editing, Writing – original draft, Supervision, Conceptualization. **Chuntida Kamalashiran:** Supervision. **Mathavadee Noonpugdee:** Supervision. **Nakarin Sivapornpan:** Supervision, Conceptualization. **Atiwut Kamudhamas:** Supervision, Conceptualization.

Declaration of Competing Interest

The authors declare no competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

No data was used for the research described in the article.

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