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Reporte de Caso

Etoricoxib-Induced Fixed Drug Eruption with Cutaneous and Mucosal Involvement: A Case Report

Eritema pigmentado fijo en brazos y mucosa oral posterior a la ingesta de etoricoxib: reporte de caso.

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ABSTRACT

Introduction: Fixed drug eruption (FDE) is a delayed hypersensitivity reaction characterized by erythematous-violaceous plaques recurring at identical anatomical sites upon re-exposure to the causative drug, with persistent residual hyperpigmentation. Etoricoxib, a widely used COX-2 inhibitor, is an increasingly recognized trigger. **Case Report:** A 49-year-old woman developed hyperpigmented plaques on the arms and oral mucosa eight hours after a single dose of etoricoxib 120 mg for acute low back pain. A clinically identical episode had occurred two years earlier at the same sites, initially misdiagnosed as herpetic infection. Diagnosis was established by temporal chronology, exact anatomical recurrence, and a Naranjo score of 10 (definite causal relationship). Management comprised drug discontinuation, oral antihistamine, and topical corticosteroid, with favorable outpatient evolution. **Conclusion:** This case illustrates etoricoxib-induced FDE with cutaneous and mucosal involvement and exact site recurrence. Early recognition, definitive discontinuation, and pharmacovigilance reporting are clinical imperatives to prevent recurrence and ensure safe alternatives.

Keywords: Fixed drug eruption; Etoricoxib; Cyclooxygenase-2 Inhibitors; Drug Hypersensitivity; Pharmacovigilance. (**Source:** MeSH-NLM

RESUMEN

Introducción: La erupción fija medicamentosa (EFM) es una reacción de hipersensibilidad retardada caracterizada por placas eritematovioláceas recurrentes en los mismos sitios anatómicos tras la reexposición al fármaco causal, dejando hiperpigmentación residual. Etoricoxib, inhibidor selectivo de COX-2, es un desencadenante. **Reporte del caso:** Mujer de 49 años desarrolló placas hiperpigmentadas en brazos y mucosa oral ocho horas después de etoricoxib 120 mg para lumbalgia aguda. Un episodio idéntico ocurrió dos años antes en las mismas localizaciones, interpretado como infección herpética. El diagnóstico de EFM se estableció por cronología temporal, recurrencia exacta y puntuación de 10/13 del Naranjo Probability Scale. El manejo incluyó suspensión del fármaco, antihistamínico oral y corticoide tópico, con evolución favorable. **Conclusión:** Este caso ilustra un EFM por etoricoxib con compromiso cutáneo y mucoso, de recurrencia exacta. El reconocimiento temprano, suspensión definitiva y reporte a farmacovigilancia son imperativos clínicos para prevenir recurrencias y garantizar alternativas seguras.

Palabras clave: Erupción fija medicamentosa; Etoricoxib; Inhibidores de ciclooxigenasa-2; Hipersensibilidad a medicamentos; Farmacovigilancia.

INTRODUCTION

Etoricoxib is a selective cyclooxygenase-2 (COX-2) inhibitor widely prescribed for musculoskeletal pain and chronic inflammatory conditions, often perceived as a safer alternative to non-selective NSAIDs in terms of gastrointestinal tolerability.(1,2) However, multiple adverse cutaneous reactions have been described in association with its use, ranging from localized eruptions to severe toxic epidermal necrolysis, prompting reassessment of its dermatological safety profile.(1,3-5)

Among these reactions, fixed drug eruption (FDE) is characterized by well-demarcated erythematous-violaceous macules or plaques that invariably recur at the same anatomical sites upon re-exposure to the causative drug and leave persistent residual hyperpigmentation.(1–4) In clinical practice, NSAIDs and particularly selective COX-2 inhibitors are recognized as frequent triggers of this delayed hypersensitivity pattern, with a growing number of reports specifically linking etoricoxib to both cutaneous and mucosal FDE.(1-4,7)

Several recent cases have documented etoricoxib-induced FDE with localized and generalized distribution, including bullous lesions and oromucosal involvement, thereby broadening the clinical spectrum associated with this agent and highlighting the importance of including it in the differential diagnosis of recurrent hyperpigmented lesions and probable drug-induced oral erosions.(1-4) Cross-reactivity with other NSAIDs, varying clinical severity, and, in the most extreme circumstances, life-threatening cutaneous toxicity have also been reported.(2,3,5)

Current drug allergy guidelines emphasize that early recognition of these patterns, timely withdrawal of the suspected drug, and identification of safe alternatives are fundamental to preventing recurrences and reducing the risk of serious complications.(6) In this context, case reports including those from Latin American primary care settings where etoricoxib is widely prescribed remain a key source for characterizing the clinical presentation, latency, and natural course of etoricoxib-associated cutaneous reactions.(1-4,7) This report describes two documented episodes of etoricoxib-induced FDE with cutaneous and mucosal involvement, diagnosed in the primary care setting after an initial misdiagnosis, with the aim of expanding recognition of this entity at the first level of care.

CASE PRESENTATION

A 49-year-old woman and university professor, with a history of myomectomy (June 2015) and regular use of tranexamic acid for metrorrhagia secondary to uterine myomatosis, presented on 12 March 2026 with acute onset of hyperpigmented plaques on the upper limbs and oral mucosa, appearing eight hours after a single dose of etoricoxib 120 mg for acute low back pain, administered concomitantly with orphenadrine 100 mg. Relevant past medical history included an adverse reaction to epidural anesthesia and tachycardia following a third dose of aspirin 75 mg in 2021. Her mother had a known hypersensitivity reaction to tramadol.

First episode (August 2024). The patient reported a clinically identical episode in August 2024 following several days of etoricoxib 120 mg. Lesions appeared on the oral mucosa (left lower lip), initially diagnosed as herpes zoster, and treated with antiviral therapy for seven days. Simultaneously, three hyperpigmented plaques appeared on the distal third of the left arm, one at the anatomical snuffbox of the right hand, and intense bilateral palmar erythema in the hypothenar regions (VAS pruritus: 8/10). Lesions resolved over 30 – 60 days with residual hyperpigmentation lasting more than one month. No causal link with etoricoxib was established at that time.

Second episode and current presentation (March 2026). Eight hours after etoricoxib 120 mg on 11 March 2026, the patient identified reappearance of lesions at anatomically identical sites. Physical examination revealed three hyperpigmented plaques on the distal third of the lateral left arm: primary lesion 1.0 × 1.3 cm, dark violaceous, well-demarcated, smooth surface; two satellite lesions 1.0 × 1.2 cm (medial) and 1.0 × 1.5 cm (lateral), less intense pigmentation, diffuse borders. A 1.0 × 1.2 cm plaque was observed at the right anatomical snuffbox. Mucosal involvement of the left lower lip, bilateral palmar thenar erythema with local burning, no genital or plantar lesions. Pruritus mild (VAS 1/10) notably lower than the prior episode. Nikolsky sign negative. (see Figure 01)

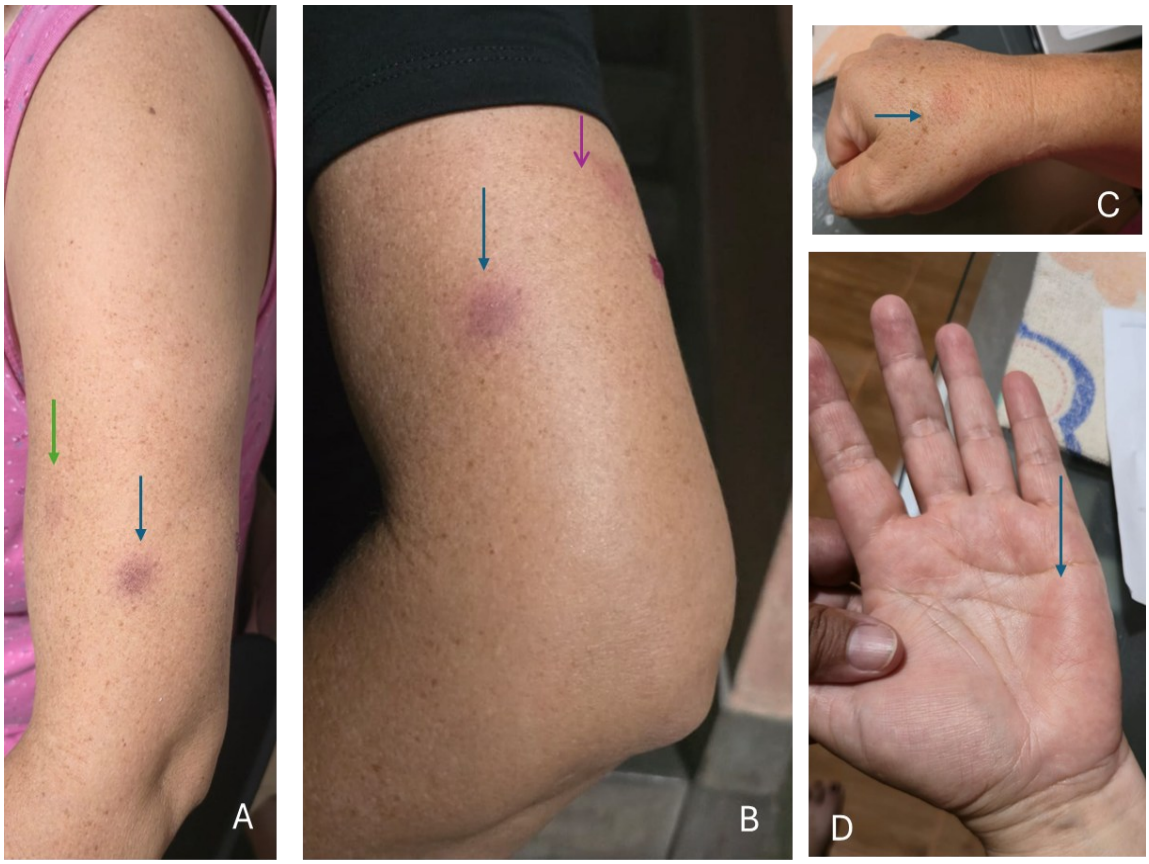

Figure 1. Etoricoxib-induced fixed drug eruption ***AB****, left arm: primary lesion 1.0 × 1.3 cm, dark violaceous, well-demarcated, smooth surface (black arrow); two satellite lesions* ***A****, 1.0 × 1.2 cm (green arrow, medial) and* ***B****, 1.0 × 1.5 cm (lateral, purple arrow), less intense pigmentation, diffuse borders.* ***C****, 1.0 × 1.2 cm plaque was observed at the right anatomical snuffbox. Mucosal involvement of the left lower lip.* ***D****, bilateral palmar thenar erythema with local burning*.

Vital signs: BP 110/65 mmHg, HR 75 bpm, RR 19 rpm, axillary temperature 36.5 °C, SpO_2 99%. Alert, oriented, hemodynamically stable, no lymphadenopathy, no hepatosplenomegaly.

Table 1. Naranjo Algorithm Adverse Drug Reaction Probability Scale in the case report.

Questions	yes	no	Score
Previous reports of this reaction	+1		
Reaction after suspected drug:	+2		
Improved on withdrawal:	+1		
Recurred on re-administration	+2		
Alternative causes:		+1	
Reaction with placebo:		+1	
Drug at toxic level:		0*	
More severe at higher dose		0*	
Similar reaction to same drug before	+1		
Confirmed by objective evidence	+1		
Total score			10

DEFINITE causal relationship (≥9 = definite); Naranjo et al., (Clin Pharmacol Ther 1981). Total Score ≥9: Definitive; Total Score 5 to 8. Probable; Total Score 1 to 4 Possible; Total Score ≤0. Doubtful (10)

***Differential diagnosis*:** Contact dermatitis excluded (no relevant contactant exposure). Recurrent herpetic infection ruled out (morphology, distribution, and absence of vesicles inconsistent). Stevens-Johnson syndrome excluded (limited extent, no epidermal detachment, negative Nikolsky sign). Orphenadrine-induced FDE excluded: orphenadrine is not a recognized FDE trigger, and exact lesion recurrence across both episodes in which etoricoxib was the common denominator firmly attributes causality to etoricoxib. No skin biopsy, patch testing, or oral provocation challenge was performed; the clinical diagnosis was conclusive, and re-exposure would represent unnecessary risk.(see table 01).

Management. Immediate and permanent discontinuation of etoricoxib. Ambulatory regimen: desloratadine 5 mg orally once daily × 7 days; betamethasone 0.05% topical cream twice daily × 7 days. No hospitalization required. Patients were instructed to avoid all selective COX-2 inhibitors. Weekly outpatient follow-up scheduled. **Follow-up at 15 days.** Satellite lesions resolved with progressive attenuation of hyperpigmentation. Primary left arm plaque persists with gradual reduction. For reference, the first episode (2024) required approximately 60 days for complete resolution. Patient adherent, with adequate understanding of permanent avoidance of the causative agent.(see table 2).

Table 2. Clinical timeline of two episodes of etoricoxib-induced fixed drug eruption.

Time point	Episode	Event / Finding
August 2024	1st	Etoricoxib 120 mg prescribed multiple doses over several days
August 2024 (8 h)	1st	Onset: left lower lip lesion + 3 arm plaques + right hand plaque + palmar erythema (VAS pruritus 8/10)
August 2024	1st	Misdiagnosis: herpes zoster antiviral therapy 7 days. No causal link to etoricoxib established.
Aug–Oct 2024 (~60 days)	1st	Resolution; residual hyperpigmentation > 30 days
11 March 2026	2nd	Single dose: etoricoxib 120 mg + orphenadrine 100 mg for acute low back pain
12 March 2026 (8 h)	2nd	Onset: identical sides left arm (×3) + right hand + left lower lip + bilateral palmar erythema (VAS 1/10)
12 March 2026	2nd	Correct diagnosis: etoricoxib-induced FDE · Naranjo score 10/13 (DEFINITE) Drug discontinued
12–19 March 2026	2nd	Desloratadine 5 mg/d + betamethasone 0.05% topical × 7 days.
27 March 2026 (Day 15)	2nd	Satellite lesions resolved; primary plaque persisting with gradual reduction

DISCUSION

The present case is consistent with an expanding body of literature documenting etoricoxib-induced FDE in high-impact dermatology, allergology, and oral surgery journals, as well as in Latin American clinical publications.(1-5,7-10) Across these reports, the clinical presentation is relatively uniform: well-demarcated erythematous-violaceous macules or plaques appearing hours to days after drug administration, exact recurrence at identical anatomical sites upon re-exposure, and resolution with persistent post-inflammatory hyperpigmentation.(1-4,9) (see Table 3) In our patient, the latency of approximately eight hours after a single 120 mg dose, together with exact recurrence of hyperpigmented plaques on the arms and oral mucosa at anatomically identical locations

to the 2024 episode, reproduces this classical FDE pattern precisely.(1-3)

The cases reported by Porr et al. and Makris et al. provide the closest clinical parallels.(1,2) Porr et al. describe a woman who developed well-demarcated plaques eight hours after a single 60 mg dose of etoricoxib, with confirmation by oral provocation challenge.(1) Makris et al. report cross-reactivity between nimesulide and etoricoxib, with bullous lesions, underscoring that sensitization may extend across chemically related or even unrelated NSAIDs.(2) Relevant to the present report is the Peruvian case documented by Dextre-Vilchez (2025), which describes etoricoxib-induced FDE with genital and mucosal involvement confirming that this adverse reaction is recognized in our region and that local pharmacovigilance data are beginning to emerge.(9)

The oral mucosal involvement in this case has been documented by Rawlings et al. and Perks et al., who report etoricoxib-induced FDE presenting as oral erosions at high risk of misdiagnosis as herpetic or idiopathic ulcerative conditions.(3,4) The initial management of our patient as a herpetic infection later corrected when the second episode disclosed the causative pattern reflects precisely this diagnostic pitfall, and underscores the value of detailed drug history review in recurrent oral lesions.(3,4)

Regarding the concomitant use of orphenadrine 100 mg during the second episode: orphenadrine, a centrally acting skeletal muscle relaxant with anticholinergic properties, is not recognized as an FDE trigger in published literature. The occurrence of clinically identical lesions at the same sites during the first episode in which orphenadrine was not documented firmly attributes causal responsibility to etoricoxib rather than to the concomitant agent.

Table 3. Published cases of etoricoxib-induced fixed drug eruption (2016–2025)

First author, year	Country	Journal (Q)	Dose / Latency	Involvement	Management	Resolution
Sousa AS et al., 2016	Portugal	An Bras Dermatol (Q1)	Etoricoxib / NR	Trunk, hand (bullous)	DC + patch test	Weeks + residual pig.
Lim JT et al., 2020 — 7 cases	Singapore	Contact Dermatitis (Q1)	60–120 mg / h–days	Multiple sites, varied	DC ± topical CS	2–6 weeks
Perks A et al., 2021	UK	OOOO (Q1)	90 mg / hours	Oral mucosa (erosions)	DC + topical CS	2–3 weeks
Makris M et al., 2024	Greece	J Clin Med (Q1)	Nimesulide → etoricoxib / h–days	Multifocal, bullous	DC + systemic CS	Several weeks
Rawlings N et al., 2024	UK	Br J OMF Surg (Q1)	90–120 mg / h–days	Oral mucosa	DC + topical CS	4–6 weeks
Mota D et al., 2025	Portugal	Dermatitis (Q1)	Etoricoxib / h–days	Generalized	DC + systemic CS	Weeks + pig.
Siriwattanasatorn M et al., 2025	Thailand	Toxicol Rep (Q1)	90 mg / 2 h	Leg, foot, arm, lumbar (bullous)	DC + systemic CS	Several weeks
Porr C et al., 2025	Romania	J Clin Med (Q1)	60 mg / ~8 h	Hand, leg (plaques)	DC + desloratadine	Weeks + pig.
Dextre-Vilchez, 2025 [9]	Peru	Iatreia (Q2)	90 mg / hours	Genital + macules	DC + topical CS	3–4 weeks

DC = drug discontinuation; CS = corticosteroid; pig. = post-inflammatory hyperpigmentation; NR = not reported; OMF = oral and maxillofacial; OOOO = Oral Surg Oral Med Oral Pathol Oral Radiol. Orange row = Dextre-Vilchez case (Iatreia, 2025).

The Naranjo probability scale yielded a score of 10/13, classifying the causal relationship as definite (score ≥9).(11) This systematic assessment supports the diagnostic conclusion even in the absence of skin biopsy, epicutaneous patch testing, or oral drug provocation challenge procedures that, while used in confirmatory series,(1,2,8,10) carry procedural risk and are generally not required when clinical diagnosis is unambiguous.(6)

From a pharmacovigilance perspective, most published etoricoxib-induced FDE cases arise from specialized services, suggesting significant underreporting from primary care settings.(3,6–9) The present report originates in a general outpatient setting and follows the sequence described by Makris et al. and others: initial misdiagnosis of the first episode, followed by pattern recognition only when a second episode occurred.(2,6) In Peru, adverse drug reactions can be reported to DIGEMID (Dirección General de

Medicamentos, Insumos y Drogas: www.digemid.minsa.gob.pe). Strengthening mandatory adverse drug reaction reporting, particularly for widely prescribed COX-2 inhibitors, is essential to generate regional epidemiological data and improve drug safety monitoring at the primary care level.

This report describes a particular case without skin biopsy, patch testing, or oral provocation challenge. As a first-person case report, the potential for reporting bias mitigated by objective clinical documentation must be acknowledged. Systematic photographic documentation of the first episode was not available, limiting longitudinal visual assessment. These limitations are notwithstanding, the definite Naranjo score (10-13), exact anatomical recurrence across two documented episodes, and concordance with the international published series support the diagnosis robustly.

CONCLUSION

This report documents two consecutive episodes of etoricoxib-induced fixed drug eruption with cutaneous involvement of the upper limbs and mucosal involvement of the lip, characterized by short latency (~8 hours), exact anatomical recurrence, and prolonged post-inflammatory hyperpigmentation. A definite causal relationship was established by Naranjo score (10-13), achieved through detailed clinical history and two-episode temporal concordance, without requiring biopsy or provocative testing. Early recognition of FDE at the primary care level is essential to prevent unnecessary re-exposure, avoid potentially more severe reactions, and ensure safe substitution of the causative anti-inflammatory agent. Clinicians should maintain a high index of suspicion for drug-induced FDE when evaluating recurrent hyperpigmented lesions or oral erosions temporally associated with NSAID use.

The absence of pharmacovigilance reporting in this case highlights a persistent gap in primary care adverse drug reaction surveillance. Healthcare providers in Peru are encouraged to report adverse reactions including those to widely used COX-2 inhibitors through DIGEMID's national pharmacovigilance system, contributing to regional drug safety monitoring and evidence generation.

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