

Tenoxicam-induced Fixed Drug Eruption Confirmed by Patch Testing

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ABSTRACT

Tenoxicam has been associated with cutaneous adverse reactions, and it is categorized as a non-steroidal anti-inflammatory drug (NSAID) within the oxicam class. Herein, we report a patient with tenoxicam-induced fixed drug eruption (FDE) confirmed with patch testing. FDE is a delayed type hypersensitivity reaction frequently caused by antimicrobials and NSAIDs. Cross-reactivity may occur among the oxicams, and alternative medications should be carefully selected. This report highlights the importance of patch testing in identifying the causal drug in FDE, and the rise in awareness of tenoxicam as a potential trigger.

Keywords: Fixed drug eruption, tenoxicam, patch testing

INTRODUCTION

Tenoxicam has been associated with cutaneous adverse reactions, and is categorized as a non-steroidal anti-inflammatory drug (NSAID) within the oxicam class (1). Non-specific rash, drug hypersensitivity syndrome, alopecia, photosensitivity, and toxic epidermal necrolysis are some of these reactions (2-5). Tenoxicam-related instances of fixed drug eruption have been documented in the literature (6). In this report, we present a case of tenoxicam-induced fixed drug eruption (FDE) confirmed by subsequent patch testing.

CASE PRESENTATION

A 42-year-old female health professional was referred to our clinic for asymptomatic lesions located on her face and right forearm. Upon dermatological examination, erythematous-violaceous and oval-shaped macules and patches measuring 5 to 15 mm were observed on the face and forearm, and these had developed approximately 6 to 8 hours after the second oocyte pick-up (OPU) procedure

conducted under general anesthesia. She had no recorded allergies but similar lesions had developed on her face in the same areas a week after the first OPU procedure. The patient's medical records indicated intravenous administration of midazolam (Midolam® 0.5%), remifentanyl (Ultiva® 0,005%), tenoxicam (Tilcotil® 1%), propofol (Propofol-Pf® 1%), and ondansetron (Zofran® 0.2%) during the anesthesia. Given the temporal correlation between the medicine administration and the onset of the lesions, coupled with their typical clinical appearance, a provisional diagnosis of fixed drug eruption was established.

Patch testing with midazolam (Midolam® 0.5%), remifentanyl (Ultiva® 0,005%), tenoxicam (Tilcotil® 1%), propofol (Propofol-Pf® 1%) and ondansetron (Zofran® 0.2%) (as is, solutions) was performed on the lesional skin and on the upper back of the patient, 6 weeks after the complete resolution of the lesions. Patch test readings were done on day (D) 2 and D3, according to ESCD guidelines (7). On D2 and D3, there were strong positive reactions with tenoxicam 1% over the lesional skin, confirm-

ing the diagnosis of FDE caused by tenoxicam (Figure 1,2). No positive reactions were observed over the lesional skin areas tested with other drugs or on the upper back. Written informed consent was obtained from the participant for permission to publish.

DISCUSSION

Fixed drug eruption (FDE) is a delayed hypersensitivity reaction that recurs at the same site upon re-exposure to a specific drug, typically characterized by erythematous

or violaceous patches, plaques and occasionally bullae (8). FDE has demonstrated a high density of intraepidermal effector-memory CD8⁺ T cells persisting in inactive lesions. Activation of epidermal memory CD8⁺ T cells through medication antigens leads to the release of cytotoxic cytokines such as interferon- γ and tumor necrosis factor- α , thus causing epidermal damage (9,10). Similarly, damage to melanocytes results in the leakage of melanin into the dermis (11).

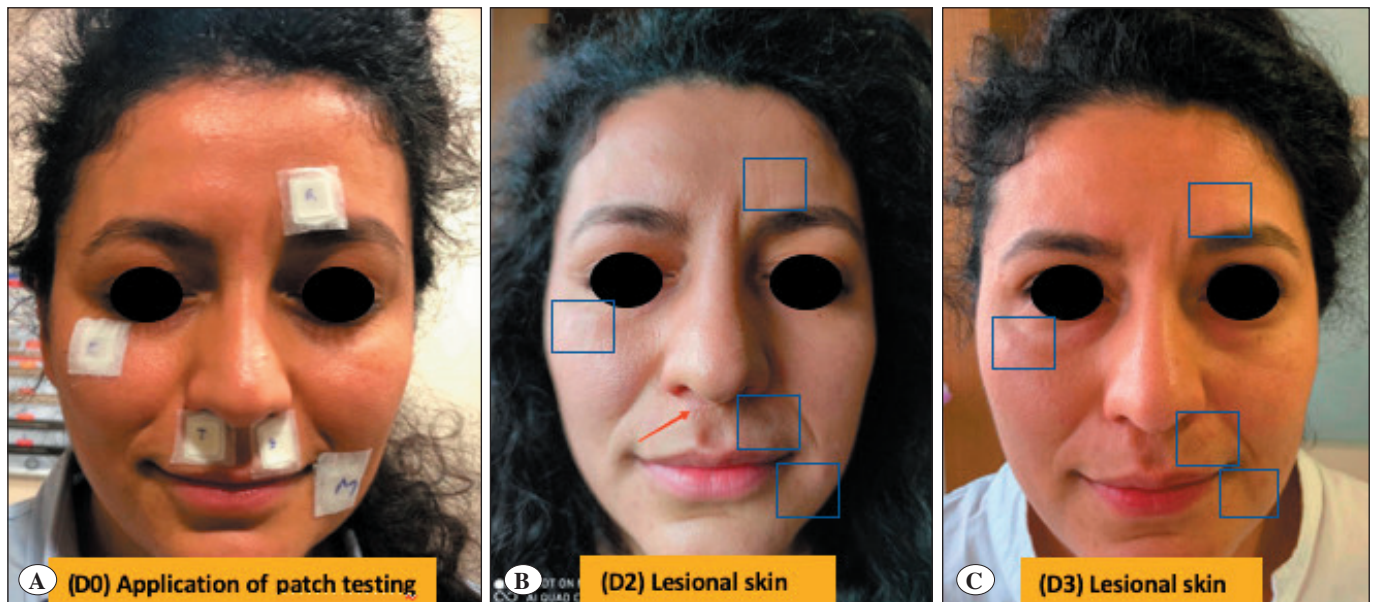


Figure 1. (A) Application of patch test to lesional skin on the face (B, C) Patch test readings: Strong positive reactions on the lesional skin on D2 and D3 (Squares indicate negative patch test sites).

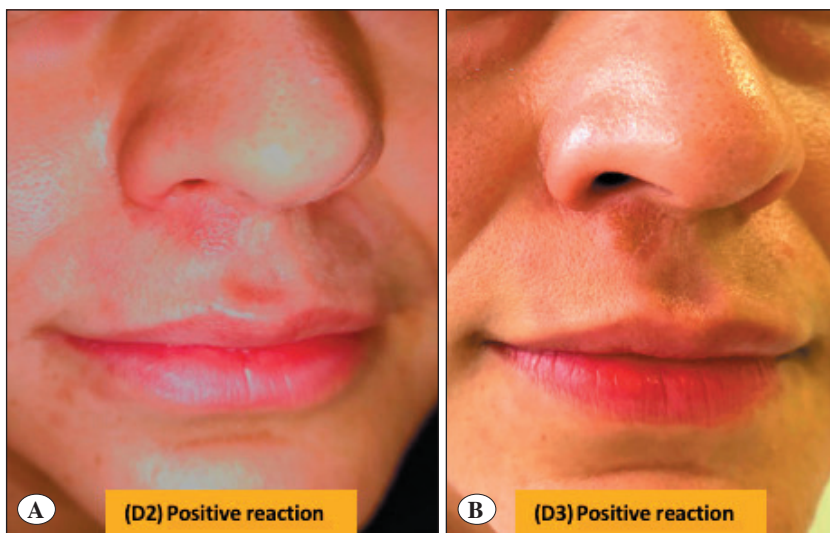


Figure 2. (A, B) Close-up of the area where strong positive reactions develop in D2 and D3, characterized by the development of vesicles and bullae on an erythematous background.

The most commonly implicated agents in fixed drug eruptions (FDE) are antimicrobials and non-steroidal anti-inflammatory drugs (NSAIDs) (8). Tenoxicam, classified as a selective cyclooxygenase-2 inhibitor within the oxicam group, has potent analgesic and anti-inflammatory effects. Oxicams have been infrequently associated with FDE (12-14).

Cross-reactivity has been documented, such as in a case where a patient experiencing FDE linked to piroxicam cross-reactivity with tenoxicam and droxicam (13). Additionally, Romdhane et al. reported positive reactions to meloxicam through patch testing or oral challenge tests in three out of seven patients who developed piroxicam-induced FDE (14). In these cases, considering the potential for cross-reactivity, opting for an agent from a different chemical group might be more judicious. There is also a reported case of FDE with polysensitivity, involving the chemically unrelated molecules tenoxicam and trimethoprim-sulfamethoxazole (6).

The presentation of this case underscores the crucial role of patch testing in precisely identifying the causative drug in FDE with atypical lesion distribution. Furthermore, it serves as a reminder that tenoxicam, despite being infrequently reported, should be considered as a potential culprit in such cases.

Conflict of Interest

The authors have no relevant financial or non-financial interest to disclose.

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Authorship Contributions

Concept: **Ozlem Akin Cakici, Andac Salman**, Design: **Ozlem Akin Cakici, Tugba Kevser Uzuncakmak, Andac Salman**, Data collection or processing: **Ozlem Akin Cakici, Tugba Kevser Uzuncakmak, Andac Salman**, Analysis or Interpretation: **Ozlem Akin Cakici, Andac Salman**, Literature search: **Ozlem Akin Cakici, Tugba Kevser Uzuncakmak, Andac Salman**, Writing: **Ozlem Akin Cakici, Tugba Kevser Uzuncakmak, Andac Salman**, Approval: **Tugba Kevser Uzuncakmak, Andac Salman**.

REFERENCES

1. Nilsen OG. Clinical pharmacokinetics of tenoxicam. *Clin Pharmacokinet* 1994;26:16-43.
2. Caughey D, Waterworth RF. A study of the safety of tenoxicam in general practice. *N Z Med J* 1989;102:582-83.
3. Aroca García MD, Luna Rodríguez C, Gallego Navarro MA, Ortiz de Solar E. Alopecia secundaria a tenoxicam. Un efecto adverso no descrito? [Alopecia secondary to tenoxicam. An undescribed adverse effect?] *Aten Primaria* 1997;20:157.
4. Santiago F, Gonçalo M, Vieira R, Coelho S, Figueiredo A. Epicutaneous patch testing in drug hypersensitivity syndrome (DRESS). *Contact Dermatitis* 2010;62(1):47-53.
5. Neagu TP, Tiglis M, Peride I, Niculae A. Toxic Epidermal Necrolysis, A Serious Side Effect of Tenoxicam Use: A Case Report. *Healthcare (Basel)* 2023;11(15):2195.
6. Ozkaya-Bayazit E. Independent lesions of fixed drug eruption caused by trimethoprim-sulfamethoxazole and tenoxicam in the same patient: a rare case of polysensitivity. *J Am Acad Dermatol* 2004;51(2 Suppl): S102-4.
7. Johansen JD, Aalto-Korte K, Agner T, Andersen KE, Bircher A, Bruze M, et al. European Society of Contact Dermatitis guideline for diagnostic patch testing recommendations on best practice. *Contact Dermatitis* 2015;73:195-221.
8. Patel S, John AM, Handler MZ, Schwartz RA. Fixed Drug Eruptions: An Update, Emphasizing the Potentially Lethal Generalized Bullous Fixed Drug Eruption. *Am J Clin Dermatol* 2020;21(3):393-9.
9. Mizukawa Y, Yamazaki Y, Teraki Y, Hayakawa J, Hayakawa K, Nuriya H, et al. Direct evidence for interferon-gamma production by effector-memory-type intraepidermal T cells residing at an effector site of immunopathology in fixed drug eruption. *Am J Pathol* 2002;161:1337-47.
10. Shiohara T, Mizukawa Y, Teraki Y. Patophysiology of fixed drug eruption: the role of skin-resident T-cells. *Curr Opin Allergy Clin Immunol* 2002;2:317-23.
11. Flowers H, Brodell R, Brents M, Wyatt JP. Fixed drug eruptions: presentation, diagnosis, and management. *South Med J* 2014;107(11):724-7.
12. Montoro J, Díaz M, Genís C, Lozano A, Bertomeu F. Non-pigmenting cutaneous-mucosal fixed drug eruption due to piroxicam. *Allergol Immunopathol (Madr)* 2003;31(1):53-5.
13. Ordoqui E, De Barrio M, Rodríguez VM, Herrero T, Gil PJ, Baeza ML. Cross-sensitivity among oxicams in piroxicam-caused fixed drug eruption: two case reports. *Allergy* 1995;50(9):741-4.
14. Ben Romdhane H, Ammar H, Ben Fadhel N, Chadli Z, Ben Fredj N, Boughattas NA, et al. Piroxicam-induced fixed drug eruption: Cross-reactivity with meloxicam. *Contact Dermatitis* 2019;81(1):24-6.