

Drug-Induced Fixed Urticaria as a Presentation of NSAID Intolerance



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We present 2 patients with a fixed drug eruption induced by nonsteroidal anti-inflammatory drugs (NSAIDs), compatible with an isolated urticarial lesion.

PATIENT 1

A 48-year-old woman had shown a 4 × 4 cm single pruritic wheal located in the right superciliary region, starting 5 minutes after the oral intake of ibuprofen 600 mg, several times during the last 2 years (Figure 1). Symptoms completely resolved in less than 6 hours without treatment. A single-blind oral challenge test with acetylsalicylic acid (ASA) was performed, resulting in a single pruritic wheal located in the right superciliary region, starting 50 minutes after the intake of ASA 125 mg (Figure 1). Cetirizine 10 mg was administered and the wheal disappeared in 15 minutes without a residual lesion.

PATIENT 2

A 50-year-old nonatopic woman, who was receiving treatment with ustekinumab for 2 years because of psoriatic arthritis, had presented several episodes of a 5 × 5 cm wheal in the right superciliary region, 30 minutes after taking orally either ibuprofen, dextketoprofen, ASA, metamizole, or diclofenac during the last 4 years (Figure 2). A single-blind challenge test with

oral diclofenac was performed, resulting in the same single pruritic wheal in the right superciliary region 30 minutes after taking it. Symptoms resolved in less than 1 hour with oral antihistamines, without a residual lesion.

Single-blind oral challenge tests with acetaminophen 1 g, meloxicam 15 mg, and celecoxib 200 mg were carried out in both patients, with good tolerance.

Lesion did not develop in our patients after diverse physical stimulations (scratching, heat, and cold) carried out during an asymptomatic period and without concomitant NSAID intake. We also proposed a skin biopsy, but both patients rejected it because of lesion location.

The presence of 1 or several well-defined cutaneous lesions appearing recurrently after contact with a drug is usually included in the dermatological group of fixed drug eruptions. We could include in this group any isolated and relapsing cutaneous lesion, although its clinical expression may differ.

When evaluating our patients, a recall urticaria was ruled out, based on the absence of any trauma or injection in the involved region. We also ruled out a solitary mastocytoma, because lesion was not suggestive and Darier's scratching sign was negative.

Our cases could be considered a type of fixed drug eruption that resembles a local form of NSAID-induced urticaria/angioedema (NIUA), according to European Academy of Allergy

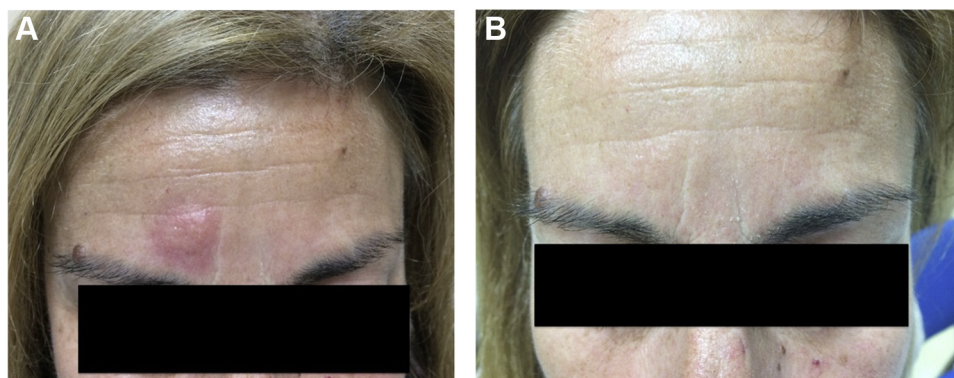


FIGURE 1. Patient 1: A, lesion after single-blind oral acetylsalicylic acid challenge; B, normal skin.

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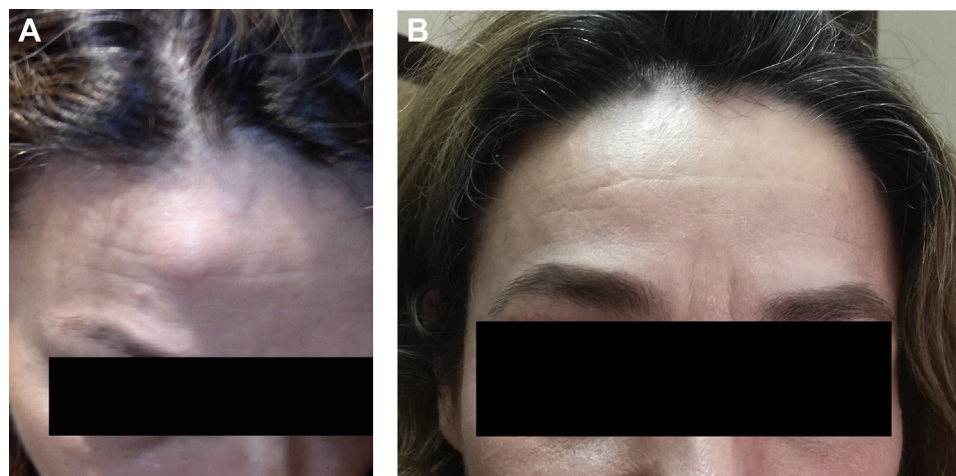


FIGURE 2. Patient 2: **A**, lesion after single-blind oral diclofenac challenge; **B**, normal skin.

and Clinical Immunology classification.¹ Cross-reactivity in this new phenotype of NSAID intolerance seems to occur, because our patients' lesions were reactivated with potent COX-1 inhibitors, while tolerating both COX-2 inhibitors and weak COX-1 inhibitors.

To our knowledge, there are only 4 other cases of fixed urticaria previously described: the first one by Feinstein et al in 1984,² due to griseofulvin; the second one by Rallis et al in 2008,³ with nimesulide tolerating piroxicam; and another 2 cases reported by Barbarroja-Escudero et al in 2015.⁴ One of them was related to mepivacaine and lidocaine, and the other one to both acetaminophen and metamizole, while tolerating other NSAIDs.

In conclusion, we report the first 2 cases of NSAID intolerance presenting as fixed drug urticaria with good tolerance to both COX-2 and weak COX-1 inhibitors. This condition could constitute a new subgroup of NIUA characterized by a recurrent

local presentation. Further investigations are needed to identify the pathogenic mechanism involved in this kind of drug adverse reaction.

REFERENCES

1. Kowalski ML, Asero R, Bavbek S, Blanca M, Blanca-Lopez N, Bochenek G, et al. Classification and practical approach to the diagnosis and management of hypersensitivity to nonsteroidal anti-inflammatory drugs. *Allergy* 2013;68:1219-32.
2. Feinstein A, Sofer E, Trau H, Schewach-Millet M. Urticaria and fixed drug eruption in a patient treated with griseofulvin. *J Am Acad Dermatol* 1984;10:915-7.
3. Rallis E, Stavropoulou E, Paraskevopoulos I. Nimesulide-induced, multifocal, urticarial fixed drug eruption confirmed by oral provocation test. *Indian J Dermatol Venereol Leprol* 2008;74:403-4.
4. Barbarroja-Escudero J, Sanchez-Gonzalez MJ, Rodriguez-Rodriguez M, Antolin-Amerigo D, Vélez D, Medina-Exposito I, et al. Fixed drug urticaria: a report of two patients. *Allergol Int* 2015;64:101-3.