

## Photoclinic



**Figure 1** **A)** On admission, the abrupt nummular change appeared bright red; **B)** Improvement of the lesion soon after the NSAID was withdrawn; **C)** The eruption evolved to a dusky-brown macule, without any treatment.

**A** 35-year-old male was admitted on October 20, 2009, tremulous and anxious, following longstanding alcoholism. Antecedent: bariatric surgery, hyperuricemia and gouty arthritis during the previous three years. He denied a history of allergy or atopic dermatitis. Admission examination was unremarkable, except for resting fine tremors of his hands. Blood counts showed leukocytes:  $7.1 (\times 10^9/L)$ , 60% neutrophils, 36% lymphocytes and 4% monocytes; erythrocytes:  $3.99 (\times 10^{12}/L)$ ; hemoglobin: 13.6 g/dL; hematocrit: 39.7%; MVC: 99 fL; MCHC: 34 g/dL; and platelets:  $171 (\times 10^9/L)$ . Serum determinations revealed glucose: 84 mg/dL; urea: 21.7 mg/dL; creatinine: 0.7 mg/dL; albumin: 3.9 g/dL; globulins: 2.0 g/dL; uric acid: 10.2 mg/dL; ionized calcium: 1.28 mmol/L; magnesium: 2.0

mg/dL; sodium: 141 mEq/L; potassium: 3.5 mEq/L; ALT: 18.9 U/L; AST: 13.4 U/L; alkaline phosphatase: 73.4 U/L; gamma-GT: 35.7 U/L; prothrombin activity: 89%; RNI: 1.05; bilirubin: 0.9 mg/dL; cholesterol: 106 mg/dL; LDL: 47 mg/dL; HDL: 34 mg/dL; VLDL: 25 mg/dL; triglycerides: 90 mg/dL; folic acid: 12.3 nmol/L; TSH: 0.62 U/mL; free T4: 0.76 ng/dL.

On October 24, he used tenoxicam because of foot arthritis. On the next day, one lesion suddenly erupted on the left hypothenar region. The patient remembered that identical change had previously relapsed at the same site, “invariably associated with elevated levels of uric acid”. The erythematous lesion was solitary and oval-shaped,  $4.5 \times 3.5$  cm (Figure 1A), with a local burning sensation. Following withdrawal of the non-steroidal anti-inflammatory drug (NSAID) and without any treatment, the eruption rapidly faded to a dusky-brown macule (Figures 1B and 1C), which became almost imperceptible when he was discharged to home, asymptomatic, ten days after admission.

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**What is Your Diagnosis?  
See the next page for diagnosis.**

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Most common presentations of cutaneous drug reactions are angioedema, erythema multiform, exanthema, urticaria and fixed drug eruption (FDE).<sup>1</sup> This term was first introduced by Brocq in 1894.<sup>2</sup> FDE is a common drug reaction that has been scarcely reported in association with tenoxicam, which may be involved in cross-reactivity,<sup>3,4</sup> and in polysensitivity.<sup>5</sup> Typical characteristics of FDE include macules, plaques, vesicles, or bullous changes that recur at the same site following each exposure to the causative drug.<sup>6,7</sup> Lesions are mainly round or oval and show well-demarcated limits; they abruptly appear and heal in few days often leaving residual hyperpigmentation.<sup>6,7</sup> Burning and pruritus are frequent claims, but lesions may be asymptomatic. Mucous membranes are less commonly affected.<sup>3,7</sup> Microscopic studies reveal necrosis of keratinocytes, nuclear pyknosis, basal layer degeneration, melanin-laden macrophages, and perivascular infiltrates of mononuclear and polymorphonuclear leukocytes in the dermis.<sup>7</sup> Diverse drugs have been associated with FDE, including: acetylsalicylic acid, allopurinol, antibiotics, anticonvulsants, belladone, cotrimoxazole, dipirone, finasteride, fluconazole, hyoscine, paracetamol, phenacetin, phenolphthalein, NSAIDs, oral contraceptives, quinine, and sedatives.<sup>6,7</sup> The pathogenesis is not well-known<sup>6</sup> but recent data emphasize the role of intraepidermal CD8+T cells with an effector-memory phenotype resident in the FDE.<sup>8</sup> The diagnosis is based on accurate anamnesis and clinical features, while provocative tests and biopsy can be confirmatory. In addition to withdrawal of the involved drug to prevent recurrences, one may prescribe topic and/or oral corticosteroids depending on the extension and severity of the lesions.<sup>3</sup>

The patient was admitted due to the effects of alcoholism, and an initial episode of gouty arthritis was controlled by immediate use of tenoxicam. Of note, eight hours after ingesting the drug, one typical lesion of FDE appeared on his left palm<sup>6,7</sup>; moreover, it rapidly faded following tenoxicam withdrawal. Another strong characteristic of FDE was the abrupt development of identical changes at the same site,<sup>6</sup> after exclusive use of tenoxicam to treat his previous onset of arthritis. Interestingly, the patient misinterpreted the role played by hyperuricemia in the present case. Rather than

the etiologic factor of the lesions, elevated uric acid caused arthritis and the painful episodes were controlled uniquely with tenoxicam. Neither analgesics nor allopurinol were associated. Similar to the description of Montoro and colleagues, the oral challenge test was not performed and the reactivity for tenoxicam (1% pet) could not be shown by a respective patch test.<sup>3</sup> The lack of a positive result constituted a major concern, and could be considered a weakness of the study. Nevertheless, recent data from a retrospective and prospective Iranian study revealed that 43.8% of negative results in re-challenge tests were performed in 150 patients with mild drug reactions,<sup>1</sup> which could be applicable to the present case. Moreover, Ordoqui and colleagues also found a negative patch test for oxycams performed on normal but previously affected skin, which indicates variable results of the test.<sup>4</sup> Furthermore, negative tests can be due to insufficient CD8+cells at the site of previous FDE.<sup>8</sup>

With the aim of prevention, the patient was fully informed about this adverse drug-effect, and was advised to carry a card for future eventual emergency information.<sup>1</sup>

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