of neutrophilic dermatosis of the hands are associated with tumors (mostly hematological in origin), and 15% of cases are associated with inflammatory bowel disease.[2] The disorder has also sporadically been associated with hepatitis C and streptococcal infection.[6] Its occurrence in patients with rheumatoid arthritis is more infrequent, and in this context, it is important to distinguish it from other neutrophilic dermatoses related with this disease, such as rheumatoid neutrophilic dermatitis, erythema elevatum et diutinum, and pyoderma gangrenosum.[7] Given the clinical similarities, a differential diagnosis with rheumatoid neutrophilic dermatitis becomes particularly relevant.[8] There are no more than 30 cases of rheumatoid neutrophilic dermatitis—first described in 1978 by Ackerman—reported in the literature. This nonparaneoplastic sudden-onset dermatosis mostly affects women with seropositive rheumatoid arthritis. It is characterized by the formation of tender erythematous nodules and papules on the hands and extensor surfaces of the limbs, mainly around the joints and adjacent areas. The histopathology study reveals an intense neutrophilic infiltrate in the dermis with a variable degree of leukocytoclasia. Rheumatoid neutrophilic dermatitis is distinguished from neutrophilic dermatosis of the hands by the absence of vasculitis. The finding of vasculitis in the latter becomes more evident as time passes after the onset of symptoms.[1,9] It is not unusual for rheumatoid neutrophilic dermatitis to resolve spontaneously or secondary to an improvement in the underlying rheumatoid disease. Other cases tend to resolve in response to treatment with dapsone.[8] The treatment of choice for neutrophilic dermatosis of the hands is systemic corticosteroid therapy using oral prednisone at doses of up to 1 mg/kg/d. Contrasting with rheumatoid neutrophilic dermatitis, there is a response rate of up to 71%. Cases that fail to respond to systemic corticosteroid therapy should be treated with dapsone or potassium iodide.[10]

In conclusion, in cases of neutrophilic dermatosis of the hands, we believe that extensive screening should be performed to exclude the possibility of neoplastic or other diseases, given that there is a rare association—as occurred with our patient—between neutrophilic dermatosis of the hands and rheumatoid arthritis-like rheumatological disorders.

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Allergic Contact Dermatitis due to Amorolfine in Nail Lacquer

Dermatitis alérgica de contacto por amorolfina en laca de uñas

To the Editor:

Allergic contact dermatitis caused by antifungal drugs is relatively infrequent despite the widespread use of these agents. A few cases of allergic contact dermatitis have been described, with imidazole derivatives as the most frequently implicated allergens.[1,2]

Amorolfine is a morpholine derivative that is structurally unrelated to any other antimycotic drug. It was originally marketed in some countries as a nail lacquer treatment for onychomycosis. Amorolfine cream has recently been made available in Europe, Asia, and South America as a treatment for fungal skin infections. To date, only 3 cases of allergic contact dermatitis attributed to amorolfine have been reported in the literature.[3-5]

A 36-year-old woman, with no relevant past history, was referred to our dermatology clinic with possible onychomycosis of the 2 great toenails that had developed over several months and that had not been treated previously. Physical examination revealed both great toenails to be distally thickened and slightly greenish

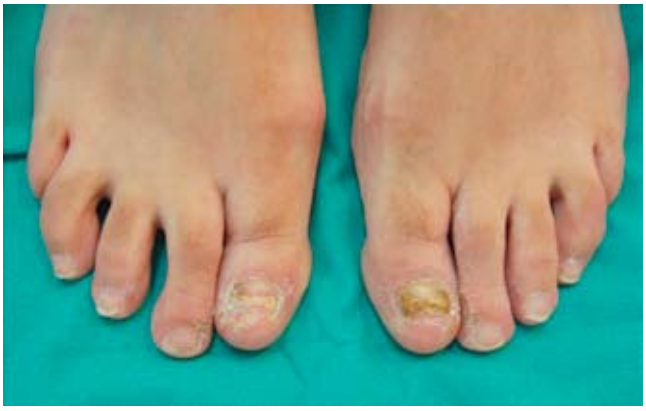

Figure 1 Scaly, erythematous lesions on both great toes.

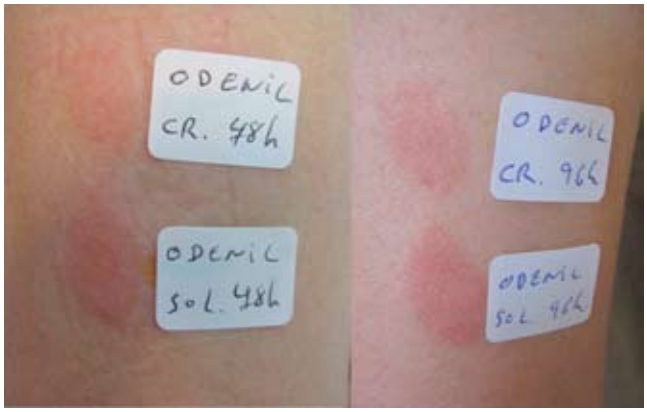

Figure 2 Patch tests performed with Odenil nail lacquer and Odenil cream.

in color. Onychomycosis or *Pseudomonas* infection was suspected and samples were taken for bacterial and fungal cultures. Despite the absence of fungal growth in the culture, given the strong clinical suspicion, topical treatment with 5% amorolfine nail lacquer (Odenil, Laboratorios Isdin, Spain) was prescribed for application twice weekly. A month after commencing treatment, the patient observed a pruritic, eczematous rash with vesicle formation on the dorsum of both great toes; a month later she came to our surgery with scaly, erythematous lesions on the dorsum of both great toes that had spread as far as the third toe of each foot (Figure 1). Treatment with the nail lacquer was suspended, and the lesions cleared up within a few days after topical treatment with hydrocortisone. Patch tests were performed using the standard Spanish Contact Dermatitis and Skin Allergy Research Group (GEIDAC) battery and Odenil nail lacquer. Results were read at 48 and 96 hours in accordance with International Contact Dermatitis Research Group (ICDRG) criteria. Tests were positive for nickel (++ on day 2 and +++ on day 4) and for Odenil nail lacquer (+ on day 2 and ++ on day 4). Patch tests were then performed with both Odenil nail lacquer (5% amorolfine, methacrylic acid copolymer, triacetin, butyl acetate, ethyl acetate, and ethanol) and Odenil cream (0.25% amorolfine, polyethylene glycol 40 monostearate, stearyl alcohol, liquid paraffin, white soft paraffin, carbomer 934P, sodium hydroxide, disodium edetate, 2-phenoxy ethanol, and purified water). Results were positive for both preparations (++ on day 2 and ++ on day 4) (Figure 2). Results were negative for 15 healthy patients used as controls for the Odenil nail lacquer and cream tests. Finally, to rule out sensitization to components in the cream and nail lacquer, patch tests were performed using the cosmetic battery of 50 allergens (Chemotechnique Diagnostics AB, Vellinge, Sweden) and 2% methacrylic acid in soft paraffin, with negative results.

Amorolfine—(2S,6R)-S2,6-dimethyl-4-(2-methyl-3-(4-[2-methylbutan-2)phenyl)propyl]morpholine—is a topically applied morpholine derivative (Figure 3) that inhibits D14 reductase and D7-8 isomerase and so blocks synthesis of ergosterol (a component of the fungal cell wall), altering the permeability of the cell membrane and so affecting fungal growth. Structurally different to other antimycotic

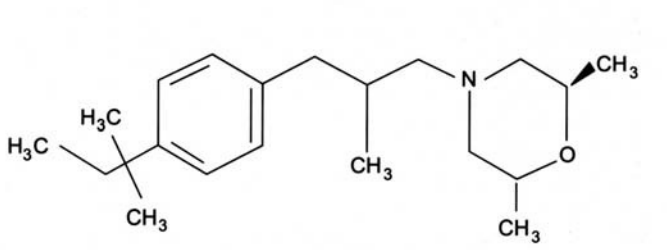

Figure 3 Chemical structure of amorolfine.

drugs, it has been marketed in a number of countries as both a cream and nail lacquer (under the Odenil, Locetar, and Loceryl brands). It is frequently prescribed as a nail lacquer treatment for onychomycosis.

A review of the literature reveals three cases of allergic contact dermatitis developing in response to a nail lacquer or cream containing amorolfine as the active ingredient[3,5]: In 1996 Kramer and Paul reported an allergic response to amorolfine in a patient using amorolfine nail lacquer and cream,[3] in 1997 Kaneko et al reported an allergic response to amorolfine cream,[4] and in 2004 Fidalgo and Lobo reported an allergic response to amorolfine nail lacquer.[5] Ours is therefore the third case of allergic contact dermatitis due to amorolfine in nail lacquer.

We believe our case to represent a genuine allergic response to amorolfine because, in the tests for sensitization, amorolfine was the only ingredient common to both the cream and nail lacquer. Although it has been proposed that 0.25% to 1% amorolfine in soft paraffin or water should be used to prepare patches, we are of the opinion that direct tests of the cream and nail lacquer (with positive results in both cases for our patient and negative results for the controls) were highly suggestive of a diagnosis of allergic contact dermatitis due to amorolfine.

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