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Delayed access and provision of dermatological care as a collateral damage of COVID-19-related fear: Allergic contact dermatitis to fluconazole

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First-line therapy for both topical and systemic mycosis includes azoles. Despite their widespread use, they rarely cause cutaneous allergic reactions.¹ We present a patient with allergic contact dermatitis localized on the feet and around the toenails, who experienced a generalized cutaneous reaction secondary to oral fluconazole, in whom a prompt dermatological visit would have anticipated the correct diagnosis.

CASE REPORT

A 54-year-old woman was referred because of an intolerable pruriginous cutaneous rash. Cutaneous examination showed that eczematous patches involved the feet and lower and upper limbs, with dystrophic and onycholytic toenails. Her history showed that the nail lesions had begun following the removal of a semi-permanent nail lacquer. Suspecting onychomycosis, the pharmacist recommended the daily application of 28% tioconazole solution (Trosyd Nail Solution, Pfizer, New York). About 20 days after, the patient developed an erythematous and vesicular

reaction, with itching on the periungual tissues. Because of fear of going to the doctor during the COVID-19 pandemic, the patient returned to the pharmacist, who, suspecting an extension of the fungal infection, suggested applying tioconazole 1% cream. After 2 days the patient developed an extended eczematous dermatitis on her feet and lower limbs. The patient called her doctor reporting a suspicion of a widespread fungal infection, and oral fluconazole and diflucortolone valerate/isoconazole nitrate cream were prescribed by phone, with a subsequent extension of the cutaneous eruption 48 hours later (Figure 1).

The patient had no previous history of allergy. She was patch tested with the baseline series of the TRUE Test (SmartPractice, Hillerød, Denmark), a medicament series (including miconazole 1% aq., econazole nitrate 1% aq., tioconazole 1% pet.; Chemotechnique Diagnostics, Vellinge, Sweden), the patient's tioconazole 28% nail solution, and diflucortolone valerate/isoconazole nitrate cream. Fluconazole was not tested as it was unavailable. Readings on day (D)2 and D4 showed positive reactions to nickel sulfate 5%, tioconazole 1%, and tioconazole 28% nail lacquer "as is" (Figure 2).



FIGURE 1 Pruriginous cutaneous rash extended to the lower limbs after tioconazole-mediated nail solution and tioconazole cream application and fluconazole systemic assumption

DISCUSSION

During the COVID-19 pandemic, medical visits have drastically decreased for non-COVID conditions and this delay in seeking care can lead to increased morbidity, as happened in our patient.² Azole antifungals are classified into two groups: imidazoles (including tioconazole, clotrimazole, econazole, ketoconazole, and miconazole) and triazoles (including fluconazole, the most representative drug). Although many cases of allergic contact dermatitis to topical tioconazole were reported between 1989 and 1996, cases have gradually decreased over time, probably due to reduced sales.³ However, recent reports show a fresh increase in cases of peringual contact dermatitis, some of which are associated with nail onychomadesis.^{3,4}

Oral antifungals, even though rarely inducing a cutaneous rash, may cause maculopapular exanthema with eosinophilia, purpuric dermatitis or erythematous maculopapular rash associated with systemic symptoms.¹ In the case of a systemic eruption, a possible previous sensitization to topical antifungals must be investigated, since oral fungal administration could occasionally elicit a maculopapular reaction or induce a cross-sensitivity effect. Cases of interaction between



FIGURE 2 Patch test positive results to 28% tioconazole solution “as is” and tioconazole 1% pet. at day 4

topical and systemic azoles have been reported.¹ Given the frequent sensitization to topical tioconazole, our case suggests that a possible generalized eruption triggered by cross-reactivity between topical tioconazole and oral fluconazole should not be underestimated.

CONFLICT OF INTEREST

The authors declare no conflict of interests.

AUTHOR CONTRIBUTIONS

Francesca Bruni: Conceptualization; data curation; formal analysis; funding acquisition; investigation; methodology; project administration; resources; software; supervision; validation; visualization; writing-original draft; writing-review and editing. **Ambra Di Altobrando:** Conceptualization; data curation; formal analysis; investigation; supervision; validation; visualization; writing-original draft. **Aurora Alessandrini:** Conceptualization; data curation; formal analysis; investigation; methodology; project administration; supervision; validation; visualization; writing-original draft; writing-review and editing. **Michela Starace:** Conceptualization; data curation; formal analysis; investigation; methodology; supervision; validation; visualization; writing-original draft; writing-review and editing. **Bianca Piraccini:** Conceptualization; data curation; formal analysis; investigation; methodology; project administration; resources; supervision; validation; visualization; writing-original draft. **Colombina Vincenzi:** Conceptualization; data curation; formal analysis; investigation; methodology; project administration; resources; software; supervision; validation; visualization; writing-original draft; writing-review and editing.

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