Cutaneous pigmented patches

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Plaques cutanées pigmentées

Case report
A previously healthy 28-year-old man presented initially for hyperpigmented round patches of 1 to 3 centimeters in diameter, located on his trunk and limbs, and evolving for a year (figure 1). The patient had no previous history of any medical condition, such as allergy or atopic dermatitis, and he denied taking any regular or occasional medication before having the skin-pigmented eruption. A skin biopsy was, subsequently, scheduled for the next day. Twenty-four hours later, the patient presented to our department for an erythematous swelling located on his old hyperpigmented patches (figure 2). Besides, he had new erythematous lesions on his limbs and genitals. He reported that he took the day before, after returning home, 150 mg of fluconazole on its own, to prevent the recurrence of pityriasis versicolor. Two hours after the drug intake, he developed the erythematous reaction. The patient remembered that he was prescribed fluconazole last year to treat a widespread pityriasis versicolor. A skin biopsy showed marked basal cell hydropic degeneration with lymphocyte tagging along the epidermodermal junction and individual keratinocyte necrosis. There were also a lichenoid infiltrate with a superficial perivascular lymphocytic infiltration and dermal melanophages.

Figure 1
Hyperpigmented patches on the anterior chest
What is your diagnosis?

Figure 2
Rounded, swollen erythematous target-like lesions on the anterior chest after fluconazole intake
**Fluconazole-induced fixed drug eruption**

These chronic pigmented round patches, which become inflammatory after that drug intake, were suggestive of fluconazole-induced fixed drug eruption (FDE). Histopathologic findings were also consistent with the diagnosis of FDE, showing keratinocyte necrosis, lichenoid infiltrate and dermal melanophages. The patient was treated with oral prednisone 30 mg daily for 5 days, relayed by a topical corticosteroid ointment, with a dramatic improvement of the erythematous reaction but pigmentation remained unchanged. He was also recommended to avoid using fluconazole. One month after the discontinuation of corticosteroids, a patch test using fluconazole (diluted at 30% in vaseline, applied during 48 hours on a pigmented lesion) was negative.

**Discussion**

FDE accounts for up to 30% of all adverse drug reactions [1]. It is characterized by single or multiple cutaneous erythematous and/or pigmented patches that occur at the same site each time the drug is administered. However, the number and size of sites may increase after each drug intake, as observed in our patient [2]. Cutaneous swelling and redness are usually seen within 30 minutes to 8 hours after exposure, as seen in our case report. Histologically, there is a lichenoid infiltrate, a basal cell vacuolization, dermal melanophages and a perivascular lymphocytic infiltrate. Common causes of FDE include sulfonamide drugs, tetracycline and nonsteroidal anti-inflammatory drugs. Fluconazole is an uncommon cause with only 20 published cases [1–4].

In our patient, besides FDE, differential diagnosis, initially, included cutaneous mastocytosis, postinflammatory hyperpigmentation and idiopathic eruptive macular pigmentation, which may share the same clinical aspect. Cutaneous mastocytosis is usually pruritic and its cutaneous biopsy shows dermal infiltration of mast cells. Postinflammatory hyperpigmentation develops generally as a sequel of a preexisting inflammatory dermatosis. In idiopathic eruptive macular pigmentation, no drug intake or inflammatory flares are noted, and histopathology reveals only melanophages and melain deposits within the upper dermis.

The originality of our case is that our patient performed a fortuitous positive “oral test” with a therapeutic dose of fluconazole on its own. He provoked, two hours later, an erythematous reaction located on his hyperpigmented macules.

Various tests may be performed to confirm the causative drug [5]. Topical test using fluconazole is a useful and safe method [6]. However, this test may be negative (as in our patient); in this case, oral challenge test (with 25, 50 or 150 mg of fluconazole) becomes helpful [7]. In oral test, the erythematous reaction seems to occur more rapidly and more aggressively by increasing the dose of fluconazole. Our patient took a therapeutic dose (150 mg), which may explain that his “oral test” was rapidly and strongly positive. The safety of the oral test for generalized forms of FDE is not clearly established.

Our patient denied initially taking any drug. This may be due to the fact that fluconazole therapy was episodic, with a drug administration interval of several months. Fluconazole is a widely prescribed antifungal agent, which is frequently used in intermittent cures. Certain patients receiving intermittently fluconazole and developing FDE, may fail to report their drug intake. We presume that this may underestimate the real prevalence of fluconazole-induced FDE. Asking a patient with FDE about any fluconazole intake should be included in the anamnesis of any FDE. If such an exposure is present, skin tests should be performed, and if negative, oral challenge test may be performed safely.

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**References**