

Letters to the Editor

mechanical injury triggered the formation of ulcers, although it is not clear whether the ulcers appeared exactly at the sites of injection.

The reactivation of herpes viruses is widely observed in DIHS.<sup>4</sup> However, this is the first case of DIHS with multiple ulcerations at multiple sites of the body caused by HSV.

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## Fixed drug eruption caused by ornidazole and fluconazole but not isoconazole, itraconazole, ketoconazole and metronidazole

Dear Editor,

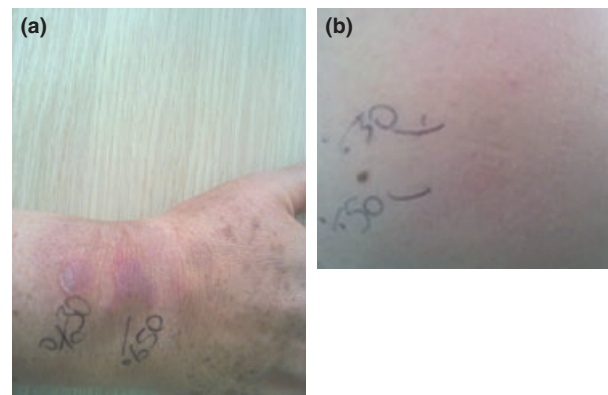
Fixed drug eruption (FDE) is characterized by round and/or oval, edematous, dusky-red macules/plaques on the skin and/or mucous membranes, accompanied by burning and/or itching.<sup>1</sup> The drugs mostly reported to cause FDE are antibiotics, non-steroidal anti-inflammatory drugs, co-trimoxazole, allopurinol, phenobarbitone and oral contraceptives.<sup>1</sup>

A 42-year-old woman presented with a recent history of hypersensitivity reaction to nitroimidazoles. She had suffered four episodes of a similar eruption at the same sites. According to her history, she had been diagnosed as having vaginal candidiasis and had been started on Fluconazole (Flucan cap, 150 mg; Pfizer, Istanbul, Turkey) 1 year prior. She reported that she had developed round, solitary, red maculae with central vesicles on the dorsal surface of both hands and elbows within 3–4 h after taking the drug. At that time, she had been diagnosed as having FDE. The maculae had faded in a few days leaving slight postinflammatory hyperpigmentation. The second episode was 3 months prior, following consumption of ornidazole (Ornicid fort, 500 mg/day; Abdi İbrahim, Istanbul, Turkey) for vaginal trichomoniasis, she had again developed three erythematous macules at the same sites and had stop taking the drug. One week after that incident, she had been seen by another gynecologist and had been given another brand of ornidazole (Ornitop fort, 500 mg/day; Toprak, Istanbul, Turkey) which resulted in recurrence of FDE at the same site. A month before admission, she had developed her last attack of FDE at previously affected sites along with itching and erythematous patches on both arms and the face within 2 h of taking fluconazole (Zolax cap, 200 mg; Sanovel, Istanbul, Turkey). She reported

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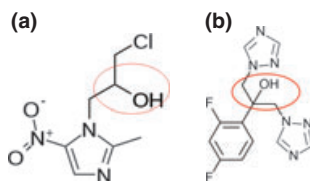
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that she had consumed itraconazole, ketoconazole and metronidazole without developing any episodes of FDE. Her physical examination showed typical oval hyperpigmentations dorsally on both hands and elbows. Occlusive patch tests at previously affected sites and on unaffected skin with 30% and 50% ornidazole (500 mg), 10% fluconazole (200 mg), and 10% isoconazole (600 mg vaginal ovule) in petrolatum were carried out and read at 48, 72 and 96 h. For patch tests, tablet forms of the drugs were crushed, vaginal ovule weighted, and mixed within white petrolatum. Patch tests were only strongly positive with 30%



**Figure 1.** (a) Positive patch tests with 30% and 50% ornidazole on affected sites. (b) Negative patch tests with 30% and 50% ornidazole on the back.

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**Figure 2.** (a) Chemical structure of ornidazole. (b) Chemical structure of fluconazole. The common component of two molecules is circled.

and 50% ornidazole on affected sites (Fig. 1) but were negative on the back, and were negative with 10% fluconazole and 10% isoconazole on both the back and previously affected sites. The patient perfectly tolerated the prescribed isoconazole vaginal ovule.

The azoles include antiprotozoal, antibacterial nitroimidazole (such as metronidazole, tinidazole, secnidazole); as antifungal compounds, imidazoles (ketoconazole, miconazole, clotrimazole) and triazoles (fluconazole, itraconazole, voriconazole) are used.<sup>2</sup> FDE induced by antiprotozoal azoles, metronidazole and tinidazole have been reported.<sup>1</sup> Ornidazole (1-chloro-3-[2-methyl-5-nitro-1H-imidazol-1-yl]propan-2-ol (Fig. 2a) is a newer nitroimidazole antiprotozoal drug, and a review of the published work on FDE due to ornidazole found only three case reports.<sup>3-5</sup> Diagnosis has been based on oral provocation with ornidazole in these cases and patch testing in 50% in petrolatum has yielded negative results in two of them.<sup>4,5</sup> Patch tests with ornidazole were positive in our patient; therefore, no oral provocation was performed. Several cases of FDE induced by fluconazole (2-[2,4-difluorophenyl]-1,3-bis [1H-1,2,4-triazol-1-yl]propan-2-ol) (Fig. 2b) have been published.<sup>1</sup> The first and last episodes of FDE had occurred with fluconazole in our patient. The diagnosis of FDE is based on history of drug exposure and examination of the lesions but the diagnosis may be supported by positive patch test, the sensitivity and specificity of which are not perfect, and therefore oral provocation test is considered gold standard. In our case, the patch test was negative with fluconazole but no confirmative oral provocation was performed, because

the temporal relation of the lesions with fluconazole use was so clear and supportive for fluconazole-induced FDE.

Cross-reactivity within members of antifungal triazole and imidazoles and between these two groups has been observed.<sup>1</sup> However, only one report demonstrated cross-reactivity between ornidazole and secnidazole but not other nitroimidazole compounds.<sup>3-5</sup> We did not check cross-reactivity with other triazoles and nitroimidazoles available in Turkey but the patient reported that she could use metronidazole without any complaint as well as itraconazole, isoconazole and ketoconazole. Our case is unique, as no cross-sensitization between antiprotozoal nitroimidazole, ornidazole and antifungal triazole, and fluconazole has emerged so far. The common component in the chemical structure of both molecules is propan-2-ol, which may be associated with cross-reaction between ornidazole and fluconazole.

Taken together, the present data support that fluconazole and ornidazole should be added to the list of the drugs inducing FDE, and cross-sensitivity among azole compounds is not necessarily always present.

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## First case of mycetoma associated with *Nocardia takedensis*

Dear Editor,

Mycetoma is a chronic and localized infection of the skin and subcutaneous tissue that sometimes involves bones or viscera, caused by either aerobic bacteria that belong to the Actinomycetales order, and characterized by tumefaction, abscess and draining sinuses tracts. It is endemic in tropical and subtropical areas, and most common in the "mycetoma belt", that includes Sudan, Somalia, Senegal, India, Yemen, Mexico, Venezuela and Colombia. *Nocardia* species are Gram-positive, weakly

acid-fast, branching bacteria whose hyphae are often fragmented to coccobacillary forms. *Nocardia* are ubiquitous in the environment and can be found worldwide as saprophytic components in fresh and saltwater, soil, dust and decaying vegetation.<sup>1</sup> It is frequently acquired after contact with soil and traumatic inoculation.

*Nocardia takedensis* was first described in 2005 as a new species of the *Nocardia* genus, closely related to *Nocardia beijingensis*, *Nocardia brasiliensis* and *Nocardia tenerifensis*. It was

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