Paradoxical Reaction During a Course of Terbinafine Treatment of Trichophyton interdigitale Infection in a Child

We describe for the first time, to our knowledge, a paradoxical reaction to terbinafine treatment in the context of dermatophyte infection due to Trichophyton interdigitale.

Report of a Case | A child weighing 30 kg and without any comorbidities and allergies and not taking any long-term medications was seen for erythematous, infiltrating, well-demarcated skin lesions located on the face, chest, abdomen, and limbs (Figure, A). Mycological culture yielded growth of Trichophyton mentagrophytes. The fungus was identified as T. interdigitale by sequence analysis of the internal transcribed spacer and the D1/D2 domains of the large-subunit (26S) rRNA gene within the rDNA cluster using the polymerase chain reaction sequencing described elsewhere.1 The patient reported frequent contact with stray cats.

Initial treatment included 125 mg of terbinafine once daily. Twelve hours after the first dose, we observed temperature elevation (39°C), chills, malaise, aggravation of inflammatory symptoms including increased erythema, edema, and pustule formation (Figure, B). These changes were accompanied by increased erythrocyte sedimentation rate (47 mm/h), elevated C-reactive protein levels (25.8 mg/L), leukocytosis (white blood cell count, 15 390/μL), eosinophilia (eosinophils, 11%), and high IgE level (7200 μg/L). (To convert C-reactive protein to nanomoles per liter, multiply by 9.524; white blood cells to ×10⁹/L, multiply by 0.001; and IgE to milligrams per liter, multiply by 0.001.) Therapy with terbinafine was discontinued for 3 days and oral prednison was administered (10 mg/d). Terbinafine therapy was reintroduced at the same dose (125 mg/d) for 6 weeks resulting in a complete resolution of skin lesions.

Discussion | Among the very few reports of paradoxical or inflammatory drug-related reactions during treatment of fungal infections are those described for Cryptococcus neoformans meningitis or disseminated paracoccidioidomycosis.3 Only 1 report to our knowledge has been published on paradoxical reactions during treatment of dermatophytosis. Nikkels et al4 described inflammatory flare-up reactions in 5 patients with dermatophyte infection undergoing antifungal therapy. In the present case, we observed high fever, chills, and malaise within 12 hours of the first dose of antifungal treatment. Elevated temperature was accompanied by intensified inflammation and pustule formation within the area of primary lesions, leukocytosis, eosinophilia, increased C-reactive protein levels, and elevated total IgE levels. The reaction symptoms prompted us to categorize it as the Jarisch-Herxheimer reaction (JHR), a well-recognized paradoxical complication of the treatment of syphilis and other infectious diseases, including leptospirosis, anthrax, meningococcal meningitis, Pneumocystis carinii pneumonia, and African trypanosomiasis.5

The present case, while sharing some features with the flare-up reaction described by Nikkels et al,4 is closer to JHR than the earlier report, and this is supported by 2 facts. First, Nikkels et al observed that the inflammatory exacerbation started 12 to 24 hours after drug intake, while a typical JHR occurs at half this time. Second, while JHR is always characterized by systemic signs (fever up to 39°C, malaise, and chills), these were present only in 2 patients with flare-up reactions (both developed the symptoms 24 hours after drug administration).4

Although eosinophilia and elevated total IgE level, as evidenced in our case, may suggest an allergy to terbinafine, successful reintroduction of the drug would negate this. The
observed reaction is also doubtfully drug related, since there were no liver test abnormalities found. The dermatophytid (id) reaction was excluded by the following observations: First, clinical lesions of id reactions are typically intensely pruritic and develop quite distantly from the site of infection. In the present case, the patient denied pruritus, and the exacerbation involved the primary lesions without production of any new ones. Second, in id reactions, no fungal forms are recovered from the lesions; in the present case, the patient's lesions yielded fungal growth. Third, over the course of id reactions, no generalized symptoms (eg, fever), as seen in this patient, are normally observed.

Altogether, this report presents an unusual case of a paradoxical reaction resembling, to some extent, the JHR, after treatment of dermatophyte infection with terbinafine.

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Complete Remission of Squamous Cell Carcinoma After Treatment With Panitumumab in a Patient With Cetuximab-Induced Anaphylaxis

A patient with locally advanced cutaneous squamous cell carcinoma (cSCC) who had had an anaphylactic reaction to an epidermal growth factor receptor (EGFR) inhibitor, cetuximab, responded to panitumumab.

Report of a Case | An 89-year-old man presented with a locally advanced cSCC of the nose that was 35 mm in diameter. The exophytic, ulcerated, necrotic tumor invaded local cartilage, but there was no metastasis (T4N0M0) (Figure, A). The large size of the lesion and difficulty in repairing the defect after excision made surgery inappropriate. In addition, the patient’s other comorbidities precluded general anesthesia. He received radiation therapy at a dose of 40 Gy in 10 fractions. The tumor progressed immediately after irradiation with a voluminous

Figure. Clinical Details of the Jarisch-Herxheimer-Like Reaction Observed in Our Study

A Before treatment
B 12 Hours after treatment

Inflammatory lesions on the abdomen and forearm of a patient on admission (A) and 12 hours after initiation of terbinafine treatment (B).