Terbinafine-Induced Subacute Cutaneous Lupus Erythematosus

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Terbinafine is a synthetic oral allylamine that is used for systemic treatment of microscopy- or culture-proven dermatophyte infections of skin and nails. It is normally well-tolerated and side effects include transient gastrointestinal symptoms and skin reactions that can occur in up to 2.3% of treated patients. Subacute cutaneous lupus erythematosus (SCLE) is a skin reaction that has been reported secondary to use of a variety of drugs. The number of reports of SCLE with terbinafine is limited. We demonstrate 2 patients in one dermatology clinic who presented with a predisposing autoimmune diathesis within 3 months of each other.

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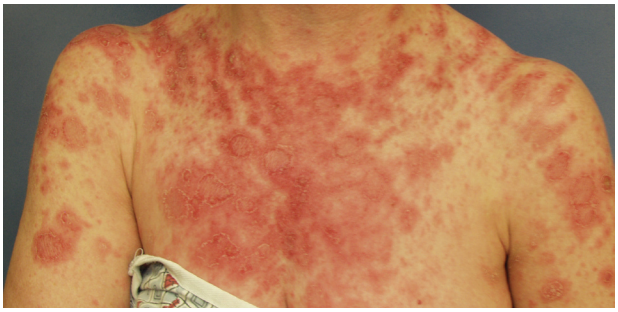
Case Reports

Patient 1—A 49-year-old white woman with a medical history of Sjögren syndrome presented to the dermatology clinic with a rash on her chest and proximal arms of 6 weeks' duration. The patient had been given terbinafine by her primary care physician for culture-proven onychomycosis 3 weeks prior to the onset of the exanthem. The patient was on no other oral medications. Within a year, she had been seen for previous eczematous rashes on the torso and shoulders, along with a biopsy-proven granuloma annulare. She had a history of positive SS-A antibodies and antinuclear antibodies (ANAs). On physical examination, the patient had polycyclic erythematous scaly patches on the arms, upper back, and face, and on the chest in the shape of a *v* (Figure). Histologic examination showed an interface dermatitis consistent with lupus or drug reaction. Serologic evaluation showed positive SS-A, SS-B, and ANA antibodies, and positive rheumatoid factor. Direct immunofluorescence was negative for IgG, IgA, IgM, C3, and fibrinogen. Initiation of plaquenil was attempted, but the patient preferred a topical regimen and the exanthem slowly resolved after 10 weeks of intermittent use of clobetasol propionate ointment and cessation of terbinafine.

Patient 2—A 68-year-old white woman with a medical history of hypertension, hyperlipidemia, reflux, and a persistently positive ANA presented to the dermatology clinic with a pruritic rash on the arms after treatment with hydrocortisone cream 1% by her primary care physician for suspected eczematous dermatitis. On physical examination, she had one large annular patch on the right arm and one small annular patch on the left arm with peripheral scale and slight induration as well as perifollicular papules. Examination of the peripheral scale was potassium hydroxide positive. A diagnosis of Majocchi granuloma was made. Terbinafine 250 mg daily was initiated with miconazole nitrate cream 2% twice daily for 2 weeks. On day 12 of terbinafine treatment, the patient presented with a spreading rash. The exanthem was an annular, slightly scaly rash with central clearing. It was located on the right lateral arm, dorsal hands, left forearm, and right dorsal distal thigh. Terbinafine was



Characteristic annular and serpiginous papulosquamous plaques on the chest and proximal arms.

continued for another week and the patient returned to the clinic presenting with polycyclic and annular, distinctly scaly, erythematous lesions on the arms, hands, chest, neck, and bilateral thighs. Clinical remission of the initial lesion resolved during this time between weeks 2 and 3. Histologic evaluation of the new lesions showed superficial and deep perivascular dermatitis consistent with polymorphous light eruption versus drug eruption. Serologic evaluation showed positive SS-A antibodies. Terbinafine was discontinued. Topical triamcinolone acetonide ointment 0.1% was initiated and the patient achieved clinical remission in 3 weeks.

Comment

Both patients demonstrated a subacute lupus reaction following treatment with terbinafine. The first case report of terbinafine-induced SCLE was published in 1998[2] and approximately 20 cases have been reported in the literature since then.[3-9] Autoimmunity has been reported as a potential predisposing factor in these cases. Because of the few cases reported, this association is not likely to be clear-cut. One proposed mechanism is that when terbinafine is deposited in the keratinocyte, it may alter the antigen structure, inducing autoantibody formation.[2] Farhi et al[3] reported a mean delay between initiation of terbinafine and symptom presentation of 5 weeks, with median remission at 8 weeks. Our 2 reported cases manifested symptoms after 2 and 3 weeks, with remission at 5 and 10 weeks, respectively. It also has been suggested that the delay in symptom remission might be attributed to the prolonged persistence of terbinafine in the stratum corneum and/or sebum.

Diagnosis is confirmed using a combination of clinical, histologic, and immunologic techniques. Drug-induced SCLE may initially present as targetoid lesions similar to lesions seen in erythema migrans. More commonly, papulosquamous; psoriasiform; or annular, erythematous, scaly lesions appear on sun-exposed areas of the skin (ie, cheeks, neck, shoulders, arms, upper chest in the shape of a *v*). Histologic patterns in SCLE show lymphocytic infiltrate at the dermoepidermal junction with basal cell liquefaction and colloid bodies. Immunofluorescence may show positive C3 and immunoglobulin. Most of the reported cases show positive anti-Ro antibodies and some anti-La positivity.

Both patients reported here showed prior anti-Ro positivity. They also had marked improvement in symptoms after terbinafine was discontinued and both patients had documented autoimmune dysfunction prior to the initiation of terbinafine therapy. Previously reported cases of terbinafine-induced SCLE also noted a correlation with autoimmune disorders. Farhi et al[3] reported this correlation in 13 patients with previously diagnosed lupus erythematosus, sicca syndrome, arthritis, photosensitivity, and Raynaud phenomenon.

There is still a paucity of data; as a result, we do not screen for ANA or anti-Ro antibodies. Larger studies are needed to analyze this association in respect to relative risk for developing this condition and any other factors that may be involved in the development of this reaction. We do suggest awareness amongst those who might be prescribing terbinafine (ie, dermatologists, family practitioners, internists, pediatricians, podiatrists). We recommend that these physicians inquire about symptoms suggestive of autoimmune disorders, connective tissue diseases, and photosensitivity. They also should warn their patients about this potential complication of terbinafine treatment. Because of this risk, physicians should initiate terbinafine therapy only after fungal infection of skin or nails is confirmed by microscopy or culture (preferably).

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