SKIN

BRIEF ARTICLE

A Subacute Cutaneous Lupus Erythematosus-Like Drug Eruption Related to Terbinafine in a Male

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ABSTRACT

Although terbinafine is generally well-tolerated, side effects occur in approximately 2-10% of patients. Patients with a history of or a predisposition to autoimmune or collagen vascular diseases may be inclined to develop drug-induced subacute cutaneous lupus erythematosus (SCLE) due to terbinafine therapy. Here, we report a case of terbinafine-induced SCLE in a male patient. However, classic SCLE most commonly affects females, and he did not have a diagnosis of or a history suggestive of a predisposition to autoimmune or collagen vascular diseases. Although the mechanism for terbinafine-induced SCLE has not been fully elucidated, we suggest that there may be distinctive mechanisms of terbinafine-induced SCLE of patients with and without a predisposition to or history of autoimmune or connective tissue diseases, which should be a focus for future research.

INTRODUCTION

Terbinafine is an oral allylamine anti-fungicidal medication that is commonly used to treat dermatophyte infections of the skin and nails.[1-3] Although terbinafine is generally well-tolerated, side effects occur in approximately 2-10% of patients.[1,2] These include cutaneous reactions of urticaria, pruritus, exanthems, papulopustular eruptions, hyperpigmentation, erythema multiforme, toxic epidermal necrolysis, acute generalized exanthematous pustulosis, pustular psoriasis, psoriasis flare, and drug-induced subacute cutaneous lupus erythematosus (SCLE).[1,4,5] Here, we report a case of terbinafine-induced SCLE in a male patient. However, classic SCLE most commonly affects females, and he did not have a diagnosis of or a history suggestive of a predisposition to autoimmune or collagen vascular diseases.[3]

CASE REPORT

An 85-year-old male presented to the dermatologist with nonpruritic and nontender red plaques on his trunk and bilateral arms and legs that had been present for 3 weeks. He had initiated terbinafine for onychomycosis approximately 7 and a half weeks prior to presentation and then discontinued after one month of treatment. He denied fevers, chills, cough, and shortness of breath. Physical examination demonstrated scattered pink to red polycyclic

annular plaques on his trunk and bilateral arms and lower legs (Fig. 1), some with overlying scale and with heme crust, but there was no ocular or oral mucosal involvement.

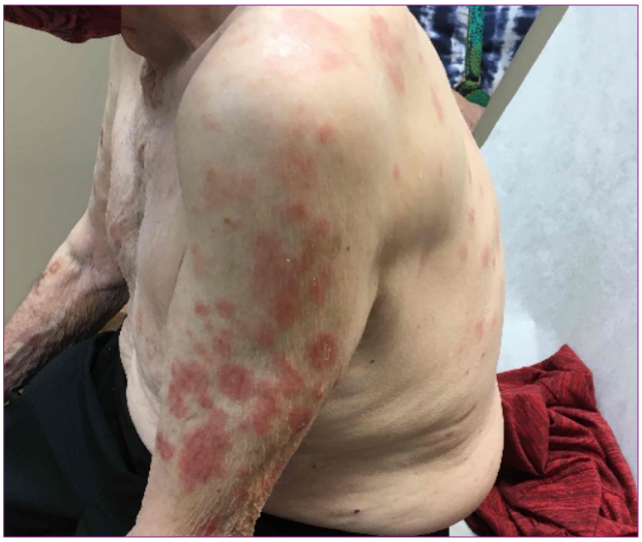

Figure 1. Terbinafine-induced subacute cutaneous lupus erythematosus. Scattered pink to red polycyclic annular plaques, some with overlying scale and with heme crust, on the bilateral arms and trunk. There were also lesions on the bilateral lower legs.

Histopathologic examination of a biopsy from the right upper arm demonstrated an interface dermatitis as well as a superficial and mid-dermal perivascular infiltrate of lymphocytes and dermal mucin and overlying parakeratosis (Figs. 2a-b). Laboratory data was significant for mild normocytic anemia, and complete metabolic panel was significant for mildly elevated creatinine (1.53 mg/dL) consistent with his baseline creatinine, but was otherwise unremarkable. Erythrocyte sedimentation rate was elevated, and IgE level was normal.

At his follow-up visit 9 days later, he demonstrated clinical improvement with the application of triamcinolone cream 0.1% to affected areas of the body twice daily and avoidance of terbinafine. However, he continued to develop additional lesions on the legs. At this time, betamethasone dipropionate cream 0.05% was prescribed to apply once daily to darker red and pink lesions with the continuation of triamcinolone cream to lighter pink lesions. He has continued to improve clinically with resolution of most lesions and diminished erythema upon follow-up approximately 3 weeks after the initiation of therapy. No further serologic studies for lupus erythematosus were completed, as there was low clinical suspicion due to the patient's age of onset of the eruption and clinical improvement with the cessation of terbinafine therapy.

DISCUSSION

Patients with a history of, or a predisposition to, autoimmune or collagen vascular diseases are inclined to develop drug-induced SCLE due to terbinafine therapy.[6,7] There have been reports of patients with systemic lupus erythematosus (SLE) who developed SCLE after terbinafine therapy.[4,6] Although an exacerbation of SLE is not commonly observed in the setting of terbinafine-induced SCLE, one case described a terbinafine-induced flare in a patient with bullous lupus erythematosus.[5,6] In addition, one case of SCLE that developed during terbinafine therapy for onychomycosis was associated with chilblain lupus.[1] There have also been reports of patients with symptoms and signs of autoimmune dysfunction who developed SCLE with terbinafine therapy.[2,7]

Terbinafine-induced SCLE has been associated with high titers of antinuclear antibodies (ANA) and the presence of anti-Ro (SS-A) antibodies, anti-La (SS-B) antibodies, and anti-histone antibodies, although the presence of anti-histone antibodies is less common.[1,3,6]

Bonsmann et al[1] observed that ANA titers and anti-histone antibodies decreased with

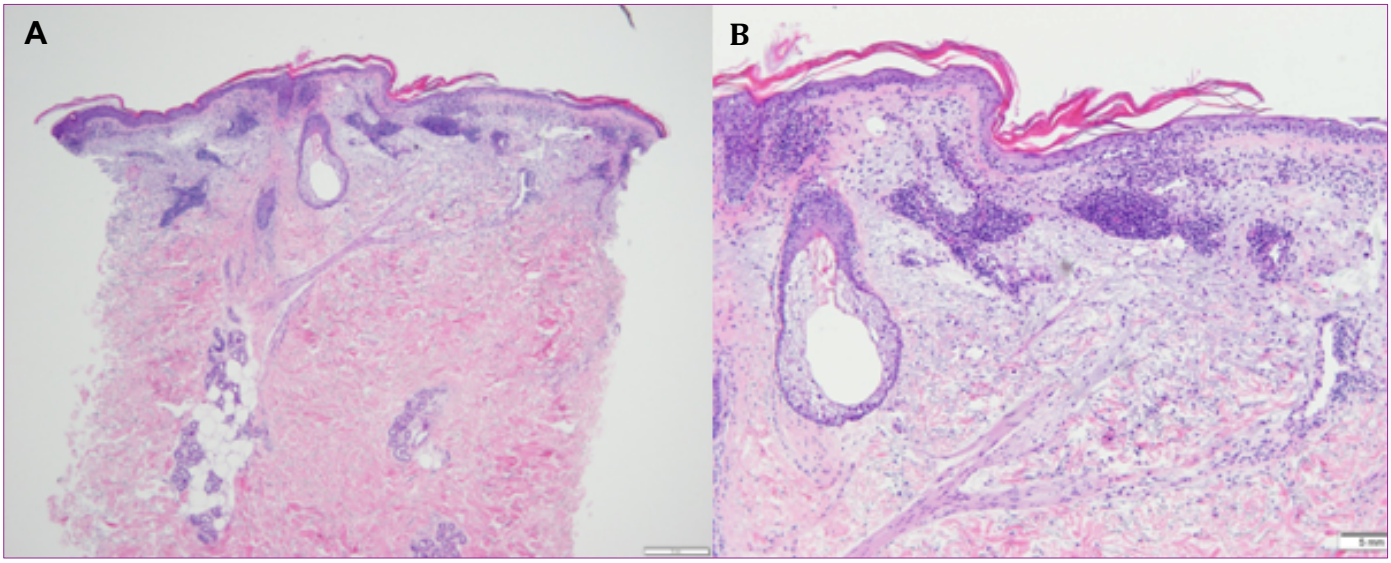

Figure 2. Histology of terbinafine-induced subacute cutaneous lupus erythematosus at **A)** low power H & E, 40x and **B)** high power H &E, 100x. Biopsy of the right upper arm demonstrated an interface dermatitis as well as a superficial and mid-dermal perivascular infiltrate of lymphocytes and dermal mucin and overlying parakeratosis.

the discontinuation of terbinafine that coincided with the resolution of the SCLE eruption in all 4 patients with terbinafine-induced SCLE.

The mechanism of terbinafine causing SCLE in predisposed patients (such as a history of systemic lupus erythematosus or SCLE, positive antinuclear antibodies, and/or presence of photosensitivity, Raynaud's phenomenon, arthralgia, myalgia, and dryness of the mucous membranes) has not been fully elucidated, but it may involve the alteration of terbinafine or its metabolites by ultraviolet radiation.[1,7] Additionally, due to the lipophilic and keratophilic nature of terbinafine, autoantibody development may occur in susceptible persons due to the deposition of terbinafine in keratinocytes and modification of the nuclear antigen structure.[1] Terbinafine may also augment the antibody-dependent, cell-mediated cytotoxic reaction in which anti-Ro autoantibodies cause keratinocyte damage.[1] In these predisposed patients, there should be special consideration about the potential for terbinafine to induce or exacerbate the disease process.[4,7]

However, it is possible that there may be a different mechanism for the development of terbinafine-induced SCLE in patients who do not have a history suggestive of a predisposition to or diagnosis of autoimmune or collagen vascular diseases, as in our patient

CONCLUSION

Although there were no serologic studies done in this case, it would be interesting to note if this patient demonstrated positive screens for autoimmune disease prior to and subsequent to the administration of terbinafine, and to further study the distinctive mechanisms of terbinafine-induced SCLE of patients with and without a predisposition to or history of autoimmune or connective tissue diseases.

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