

A case of Erythroderma following Terbinafine therapy

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Abstract

Background: The onset of cutaneous lupus erythematosus may be associated with the administration of a variety of drugs. Terbinafine, an oral antifungal agent, which rarely causes cutaneous eruptions, has been implicated as the cause or exacerbation of cutaneous lupus erythematosus in several patients.

Case: A 52-year-old female patient had received oral terbinafine for onychomycosis. The patient had a family history of lupus, but no personal history. Six weeks after initiating treatment with terbinafine the patient developed cutaneous lupus which was diagnosed clinically and by histology. She developed an erythrodermic rash. Immunological studies showed elevated titres of anti-nuclear antibodies. Following discontinuation of terbinafine therapy and under the treatment of systemic and topical steroids, a slow resolution of the eruption was noted over several weeks.

Conclusions: This report, along with previous cases described, suggests the association between terbinafine therapy and the onset or exacerbation of SLE often occurring in a patient with history of systemic lupus erythematosus or SLE.

Key words: SLE, erythroderma, drug reactions

Background

Terbinafine, an oral antifungal agent, is an effective and common treatment for dermatophyte toenail onychomycosis (1). Cutaneous systemic lupus erythematosus is rare and has been listed in the British National Formulary as a 'rare or very rare' side effect. Terbinafine has been linked to being the cause or exacerbating cutaneous lupus erythematosus in several patients (2).

It is diagnosed that cutaneous systemic lupus erythematosus is drug induced when the clinical and immunological testing are similar to idiopathic lupus in a patient with no previous history so thus relating it to the drug taken (3).

The first case of drug-induced systemic lupus erythematosus was described in 1945 (4). A distinguishing feature of drug related cutaneous lupus is the symptoms progressively resolving on stopping the offending drug and a relapse on re-exposing the patient to the same drug.

Cutaneous systemic lupus erythematosus can rarely present as erythroderma which is an intense and usually widespread reddening of the skin due to inflammatory skin disease first described by Von Hebra in 1868. The erythrodermic state is of great concern because of the dysmetabolism it creates (5). It can lead to death even when handled well hence an accurate diagnosis is crucial. A detailed outline of the patient's history to elicit possible triggering events particularly drug taken is therefore pertinent and there is a need for clinicians to be aware of this.

In this case we describe a patient who developed erythroderma as a result of lupus triggered by Terbinafine therapy for toenail onychomycosis.

Case

We present a 52 year old female patient of mixed black and white ethnicity who presented to her family physician with a widespread erythematous rash. Her only medical concern was toenail onychomycosis proven on microscopy. She had been started six weeks previously on Terbinafine at a dose of 250mg once daily. She was on no other medication, had no medical history, was a non-smoker and didn't drink alcohol. She had a family history of lupus as her mother had been diagnosed with the condition 20 years previous and was established on Methotrexate.

She described an intermittent pruritic rash for two weeks that developed until most of her skin was erythematous and inflamed. She thought the itching was related to a new shampoo she had started using but it didn't seem to ease on stopping usage. In fact, the pruritus worsened until she was unable to work or sleep. On examination she had a severe red inflammation of more than 90% of her skin including swollen eyelids. Some areas of her skin were oozing and other areas were lichenified. All of the skin examined was warm to touch. Her heart rate, temperature, respiratory rate and blood pressure were within normal parameters.

She was admitted to a dermatology ward. It was clear she had erythroderma and the differential diagnoses were that it was secondary to contact dermatitis or a drug eruption pending results. Her Terbinafine was discontinued on the ward, and her fluid balance was monitored. She was started on oral prednisolone 30mg and topical Dermovate once a day, a soap substitute and wet wrap therapy. She was also prescribed oral Flucloxacillin 500mg four times a day for 7 days and Hydroxyzine 25mg at night. Improvement was progressive over days and weeks.

Her white cell count and eosinophils were raised on admission. Immunological studies showed elevated titres of anti-nuclear antibodies. Her skin biopsy showed nonspecific inflammation on histopathology. Based on her test results and history she was diagnosed with erythroderma secondary to cutaneous lupus erythematosus triggered by Terbinafine therapy.

She made complete recovery and discharge was made after six weeks on oral Hydroxychloroquine.

Discussion

It is intriguing that black people or those of African descent are affected more with SLE. Although it is not known why, they appear to be more susceptible to it. We also know that the course and severity vary and often those of African descent suffer more severe disease (6). It is relevant thus that our patient was of mixed heritage, her mother being black. This perhaps made her more susceptible. In addition, a family history of SLE is associated with a clearly raised risk of developing SLE (7).

SLE due to drug reaction is rare representing 6% to 12% of all lupus cases (8). This case is important because in the literature Procainamide and hydralazine have been shown to have the highest incidence of causing drug induced SLE and other drugs with definite association with DIL include interferon-alpha, minocycline, isoniazid, rifampin, phenytoin, penicillamine, quinidine, phenytoin, methyl dopa, chlorpromazine, carbamazepine, ethosuximide, propylthiouracil, and sulfasalazine (9). However there have only been a few cases linking Terbinafine with drug induced SLE (2). Thus more cases like this and more in depth research providing more substantial links is necessary.

As in this case, the research supported a diagnosis of drug induced cutaneous SLE on clinical appearance and the resolution of symptoms with the withdrawal of the offending medications (10,11). Immunological testing should show a positive ANA autoantibody; usually a homogenous pattern is present, although the speckled pattern has been reported (9).

The backbone of treatment is understanding the link between the offending drug and the subsequent symptoms, hence discontinuing it. A positive ANA on its own does not require the cessation of the drug but the patient will require close monitoring (9).

The use of systemic steroids in more severe cases is supported in literature although caution is often advised if there is any query as to whether erythroderma was caused by psoriasis due to the risk it may cause worsening of their psoriasis (12).

As with our case above, even though the symptoms of drug induced SLE usually resolves within a few weeks of discontinuing the drug, the autoantibodies can stay positive for several months to years, and their presence alone shall be a reason for immunosuppressive therapy (9). Moreover, the positive autoantibody along with her family history and likely underlying susceptibility supports our patient continuing on Hydroxychloroquine, a disease modifying agent.

Conclusion

This case report indicates that there is an association between Terbinafine and developing cutaneous SLE particularly in susceptible patients. Previous reports have shown susceptible patients to be those with a personal history of SLE but we present a case where the susceptible patient could be someone with a significant family history. Thus this report emphasises the importance of clinicians eliciting an excellent history.

We recommend that patients with a known drug allergy that caused cutaneous SLE should be made aware that they should avoid the drug forever, and if their reaction was severe whereby they develop erythroderma, they should wear a drug alert bracelet.

References

1. Gupta AK, Lynde CW, Konnikov N. Single-blind, randomized, prospective study of sequential itraconazole and terbinafine pulse compared with terbinafine pulse for the treatment of toenail onychomycosis. *J Am Acad Dermatol.* 2001 Mar;44(3):485-91. doi: 10.1067/mjd.2001.110644. PMID: 11209119.
2. Kalińska-Bienias A, Kowalewski C, Woźniak K. Terbinafine-induced subacute cutaneous lupus erythematosus in two patients with systemic lupus erythematosus successfully treated with topical corticosteroids. *Postepy Dermatol Alergol.* 2013;30(4):261-264. doi:10.5114/pdia.2013.37038
3. Marzano AV, Vezzoli P, Crosti C. Drug-induced lupus: an update on its dermatologic aspects. *Lupus.* 2009 Oct;18(11):935-40. doi: 10.1177/0961203309106176. PMID: 19762393.
4. Hoffman BJ. Sensitivity to Sulfadiazine resembling acute disseminated lupus erythematosus. *Arch Derm Syphilol.* 1945;51(3):190-192. doi:10.1001/archderm.1945.01510210032007
5. Okoduwa C, Lambert WC, Schwartz RA, et al. Erythroderma: review of a potentially life-threatening dermatosis. *Indian J Dermatol.* 2009;54(1):1-6. doi:10.4103/0019-5154.48976
6. Lau CS, Yin G, Mok MY. Ethnic and geographical differences in systemic lupus erythematosus: an overview. *Lupus.* 2006;15(11):715-9. doi: 10.1177/0961203306072311. PMID: 17153840.
7. Constance Jensina Ulf-Møller, Jacob Simonsen, Kirsten Ohm Kyvik, Søren Jacobsen, Morten Frisch. Family history of systemic lupus erythematosus and risk of autoimmune disease: Nationwide Cohort Study in Denmark 1977–2013, *Rheumatology*, Volume 56, Issue 6, June 2017, Pages 957–964,
8. Chang C, Gershwin ME. Drug-induced lupus erythematosus: incidence, management and prevention. *Drug Saf.* 2011 May 1;34(5):357-74. doi: 10.2165/11588500-000000000-00000. PMID: 21513360.
9. Solhjo M, Bansal P, Goyal A, et al. Drug-Induced Lupus Erythematosus. [Updated 2021 Jan 27]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK441889/>
10. Kelly AS, De la Harpe Golden P, D'Arcy C, Lally A. Drug-induced lupus erythematosus secondary to pifenedione. *Br J Dermatol.* 2018 Jun;178(6):1437-1438. doi: 10.1111/bjd.16246. Epub 2018 Apr 6. PMID: 29266198.
11. Sarkar R, Paul R, Pandey R, Roy D, Sau TJ, Mani A, Ruia AV, Mondal J. Drug-induced Lupus Presenting with Myocarditis. *J Assoc Physicians India.* 2017 Jun;65(6):110. PMID: 28782328.
12. Balak DM, Hajdarbegovic E. Drug-induced psoriasis: clinical perspectives. *Psoriasis (Auckl).* 2017 Dec 7;7:87-94. doi: 10.2147/PTT.S126727. PMID: 29387611; PMCID: PMC5774610.