Response to Gu et al's "Treatment-resistant dermatophytosis: A representative case highlighting an emerging public health threat"

To the Editor: A complementary case to Gu et al's[1] case identifying treatment-resistant dermatophytosis as an emerging public health threat has been identified.[1] Recent literature indicates a global rise in resistance of *Trichophyton rubrum* and *Trichophyton mentagrophytes*, known causes of tinea infections, to terbinafine. Gu et al[1] demonstrated a case of resistant *T. rubrum* in the United States, but to the authors' knowledge, resistance of *T. mentagrophytes* has not been reported. Resistance poses an alarming challenge due to the limited availability of systemic antifungals. Additionally, a potential long-term consequence of untreated tinea infections is postinflammatory hyperpigmentation, particularly in patients with darker Fitzpatrick skin types. We describe a case of terbinafine-resistant tinea corporis caused by *T. mentagrophytes*.

A 50-year-old man, Fitzpatrick skin type IV, with no pertinent past medical history, presented with annular, scaling plaques on the upper and lower extremities and was clinically diagnosed with tinea corporis. Oral terbinafine 250-mg daily was prescribed. After a 2-month course of terbinafine, he returned to the clinic with a worsening clinical presentation (Fig 1). Biopsy of a right arm plaque was obtained, and cultures revealed *T. mentagrophytes*; PAS stain identified fungal elements consistent with tinea corporis. Second-line treatment, itraconazole 200-mg daily for 2 weeks in addition to topical ciclopirox, was then prescribed. He was contacted 3 weeks following the initiation of this regimen, and he reported complete resolution of all lesions. However, he noted extensive dark patches in previous lesional areas, consistent with postinflammatory hyperpigmentation.

Terbinafine-resistant *T. rubrum* has been documented in the United States,[1] and resistant *T. mentagrophytes* has been reported in India, Germany, Poland, and Iran. The mechanisms underlying reduced susceptibility to *T. rubrum* have been correlated with nonsynonymous mutations in

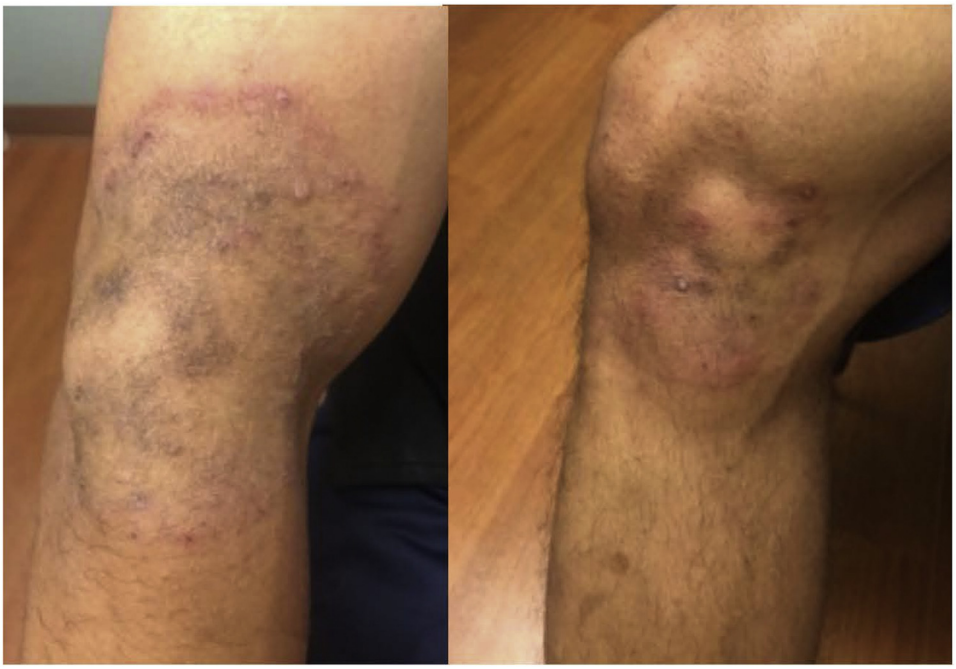

Fig 1. Tinea corporis: Right mid arm and medial knee following 2 months of oral terbinafine treatment.

the SQLE gene at varying amino acid positions: Leu393, Phe397, Phe415, and His440.[2] A study in Poland collected 20 clinical isolates of terbinafine-resistant *T. mentagrophytes* with resistant/reduced susceptibility to azoles from different regions of Poland and identified that 50% were resistant due to a Leu397Phe substitution similar to treatment-resistant *T. rubrum*.[2] Another study recruited 402 patients from 8 locations in India to determine the prevalence of in vitro resistance to terbinafine in dermatophytes and to discover mutations in the SQLE gene.[3] *T. mentagrophytes* ITS Type VIII was the dominant pathogen with 91% of the *T. mentagrophytes* isolates grown on terbinafine agar, demonstrating a Phe397Leu substitution,[3] consistent with the findings in the Polish study. Other studies that suggest mutations involving efflux pumps due to the disruption of the MDR2 gene render isolates more susceptible to terbinafine,[2] implying a potential role in terbinafine resistance.

Given the limited selection of antifungals, it is paramount to report resistant cases to highlight the severity of this growing trend. Mitigation proposals include good skin hygiene, proper dosing and duration of antifungals, susceptibility testing, and combination therapy (ie, 2 systemic antifungals, a systemic and topical antifungal, and/or a topical keratolytic).[4] Delay of diagnosis and treatment, as in the case of *T. Mentagrophytes* resistance, can lead to worsening postinflammatory hyperpigmentation, particularly in patients with skin of color, due to long-standing inflammation.

Manar T. Edriss, BS,[a] Jennifer J. Parker, MD, PhD, MPH,[b] and Ellen N. Pritchett, MD, MPH[c]

From the Wayne State University School of Medicine, Detroit, Michigan,[a] the Department of Dermatology, Temple University Lewis Katz School of Medicine, Philadelphia, Pennsylvania,[b] and the Department of Dermatology, Howard University College of Medicine, Washington, DC.[c]

Funding sources: None.

IRB approval status: Not applicable.

Key words: dermatophyte; tinea; terbinafine resistance; Trichophyton *species;* Trichophyton mentagrophytes.

Correspondence to: Ellen N. Pritchett, MD, MPH, Department of Dermatology, Howard University College of Medicine, 2041 Georgia Ave, N.W., Towers Building Suite 4300, Washington, DC 20060

E-mail: ellen.pritchett@howard.edu

Conflicts of interest

None disclosed.

REFERENCES

1. Gu D, Hatch M, Ghannoum M, Elewski BE. Treatment-resistant dermatophytosis: A representative case highlighting an emerging public health threat. *JAAD Case Rep*. 2020;6(11):1153-1155. https://doi.org/10.1016/j.jdcr.2020.05.025
2. Gnat S, Łagowski D, Nowakiewicz A, Dyląg M, Osińska M. Complementary effect of mechanism of multidrug resistance in Trichophyton mentagrophytes isolated from human dermatophytoses of animal origin. *Mycoses*. 2021;64:537-549. https://doi.org/10.1111/myc.13242
3. Ebert A, Monod M, Salamin K, et al. Alarming India-wide phenomenon of antifungal resistance in dermatophytes: a multicentre study. *Mycoses*. 2020;63(7):717-728. https://doi.org/10.1111/myc.13091
4. Pai V, Ganavalli A, Kikkeri NN. Antifungal resistance in dermatology. *Indian J Dermatol*. 2018;63(5):361-368. https://doi.org/10.4103/ijd.IJD_131_17

https://doi.org/10.1016/j.jdcr.2021.12.044