

# Treatment-resistant Tinea Corporis: A case report highlighting an ensuing public health crisis

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June 7, 2023

## Introduction

Fungal infections, most commonly caused by the dermatophytes species, are one of the most common skin conditions. Historically, these infections have been treated with antifungals such as terbinafine, fluconazole, and itraconazole. Within the past two years, there has been a rise in the incidence of fungal infections resistant to these once effective therapies, particularly emerging in India (1). We now see the spread of the “Indian epidemic” of recalcitrant cases of fungal infections to skin of color in other parts of sub-continental Asia, particularly Pakistan (2). We report a rare case of resistance to oral griseofulvin, terbinafine, and fluconazole in the treatment of tinea corporis.

## Case report

A 60-year-old male with a four year history of a relapsing and remitting itch presented with exacerbation of the itch for the past seven months to a tertiary care center. The rash had spread from the anterior chest to the abdomen, legs, and groin. The patient was initially treated by his general practitioner with mild and moderate topical steroids and topical clotrimazole, which temporarily subsided the itching and reduced the inflammation of the lesions. However, he reported that the lesions would erupt soon after discontinuing the steroid and antifungal creams, resulting in increased inflammation, pruritus and more widespread distribution. The patient continued to seek medical help from various doctors but experienced little to no improvement in his condition. He tried griseofulvin 150mg and terbinafine 250mg daily for five months without any relief. Griseofulvin and terbinafine were discontinued, and daily oral fluconazole 150mg was initiated, which also provided no relief after a month of use. Despite increased efforts to maintain personal hygiene, including showering two to three times per day and using antibacterial soaps, the patient found no relief. For the past month, the patient had been using first-generation oral antihistamines for symptomatic relief. He now states that he has developed dependence as he cannot experience undisturbed sleep without taking his nightly dose.

The patient appeared extremely distressed due to his symptoms and the financial burdens that accompanied his series of failed treatment trials. On examination, there were multiple coalescing irregularly-shaped, centrally clear lesions with erythematous, raised borders distributed across his body (Figures 1). He presented with no associated symptoms that may signify another annular skin eruption, such as subacute cutaneous lupus erythematosus, granuloma annulare, and erythema annulare centrifugum. Viral serology profile, sedimentation rate, antinuclear antibody test, and immunodeficiency workup were unremarkable. Potassium hydroxide preparation from skin scrapings revealed segmented hyphae. Subsequently, skin scrapings were cultured on two separate occasions, and in both instances, *Trichophyton rubrum* was recovered. At a three

month follow-up, the patient still presented with itch and multiple coalescing irregularly shaped lesions with centrally clear areas and erythematous, raised borders distributed across his body. At this time, molecular identification using PCR was performed, which confirmed *Trichophyton rubrum* as the causative agent. In vitro susceptibility testing was conducted and the strain exhibited susceptibility to itraconazole. Treatment with itraconazole was initiated. At a two month follow-up, the patient appeared content and exhibited clinical improvement.

## Discussion

Dermatophytosis is considered a mild skin infection that is prevalent throughout the world. The availability of various effective antifungal treatments have made the management of dermatophytosis feasible and effective. In India, a surge in the number of resistant fungal infections has become a major health concern and termed the “Indian epidemic” (2). Resistance to terbinafine in India has been well studied using molecular identification, phylogenetic analysis, in vitro susceptibility testing, and SQLE gene analysis. In 2018, Singh et al presented a series of 20 terbinafine-resistant *T. interdigitale* isolates obtained predominantly from cases of tinea corporis and tinea cruris in Delhi, India (3). A 2018 in-vitro study in India also shows antifungal resistance to griseofulvin (4). In the past three years, we see the emergence of dermatophyte infections resistant to antifungals in Pakistan and America as well (1,2). In Northern and Western Pakistan, studies report resistance to fluconazole but no resistance to nystatin (5). In this region of Pakistan, the prevalence of resistance was greater among male children in rural areas (5). In the Southern Punjab province of Pakistan, resistance to azole and polyene has been documented, most prevalent amongst females aged 21 to 30 years old (6). The one reported case of treatment-resistant *T. corporis* in the United States shows resistance to terbinafine but sensitivity to fluconazole, griseofulvin, and itraconazole (1).

In-vitro resistance to antifungals can be due to primary or secondary causes. Primary resistance occurs when an organism has an intrinsic, natural resistance to the antifungal. Secondary resistance occurs after the organism has been exposed to the antifungal and acquires resistance by undergoing specific mutations (2). A 2018 in-vitro study in India used broth microdilution assay for dermatophytes antifungal susceptibility testing and recorded MIC50 and 90 values for terbinafine, fluconazole, itraconazole, ketoconazole, voriconazole, and amphotericin B. The results of this study concluded that tinea corporis treatment failure may be attributable to the intrinsic virulence of dermatophytes species and the host fungal interaction that helps fungi evade immune response from the host, rather than to secondary antifungal resistance (7). Therefore, they recommend the terminology “recalcitrant infection” rather than “resistant cases.” Similar in-vitro studies and antifungal susceptibility testing should be performed in Pakistan and other parts of the world so that the exact cause of treatment failure can be elucidated and addressed. Dermatophytoses caused by resistant *Trichophyton indotineae* stains have been observed in parts of Europe. These strains were initially detected in India and later spread to other parts of South Asia (8). Besides resistance to cutaneous fungal infection, resistance to invasive fungi was also observed during the COVID-19 pandemic and it was responsible for increased morbidity and mortality in patients suffering from COVID-19 in India (9). Resistance in cases of invasive fungi during the pandemic was attributable to injudicious use of medications (9).

Resistant cases will demand expensive care at more equipped healthcare facilities and invasive antifungal therapies that were once reserved for immunocompromised patients, which will inevitably be accompanied by additional side effects. Newer antifungals will need to be developed to combat resistant cases. This case report aims to increase awareness amongst dermatologists and researchers about the ensuing public health crisis of treatment-resistant tinea corporis infections that are currently disproportionately affecting skin of color and demonstrate the potential of targeting socioeconomically disadvantaged communities.

## Figure Legends

**Figure 1** . Anterior chest showing multiple coalescing irregularly shaped, centrally clear lesions with erythematous, raised borders.

## References

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