Medical Mycology Case Reports 49 (2025) 100715

Contents lists available at ScienceDirect

Medical Mycology Case Reports

journal homepage: www.elsevier.com/locate/mmcr

The association of *Yarrowia lipolytica* with onychomycosis

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A B S T R A C T

Onychomycosis, a common fungal nail infection, is typically caused by dermatophytes or *Candida* species, but rare fungal pathogens can also be involved. We describe a 20-year-old woman with persistent nail shedding who was unresponsive to standard antifungal treatments. Microscopic nail examination, fungal culture, and ITS sequencing repeatedly identified the presence of *Yarrowia lipolytica* (formerly *Candida lipolytica*), a dimorphic yeast more often associated with systemic bloodstream infections and not previously identified in patients with onychomycosis. Susceptibility testing revealed the resistance of *Y. lipolytica* isolates to multiple antifungal azoles, complicating future treatment strategies for the patient. Commonly found in hydrocarbon-rich environments and an important organism for biotechnology, *Y. lipolytica* has industrial applications but is also capable of causing opportunistic infections in vulnerable patient populations. This case highlights the importance of thorough microbial identification and susceptibility testing in cases of treatment-resistant onychomycosis.

1. Introduction

Onychomycosis, a chronic fungal infection of the nail, is estimated to affect ~4 % of people worldwide, with poor treatment outcomes and high recurrence rates [1,2]. The majority of these cases affect the toenails, rather than the fingernails, with common symptoms including nail malformation, such as thickening, crumbling, and discoloration. The condition is often chronic, leading to ingrown toenails and nail loss. Risk factors include, but are not limited to, old age, diabetes, tinea pedis, and a weakened immune system [3]. Nail infections are typically caused by filamentous fungi, particularly the dermatophyte species of the *Trichophyton* genus, resulting in tinea unguium. Other fungi have also been found to cause onychomycosis, including yeasts (e.g., *Candida* spp.) and saprophytic molds (e.g., *Fusarium* spp., *Aspergillus* spp.).

2. Case presentation

A 20-year-old white woman from the state of Idaho in the United States presented with chronic proximal subungual onychomycosis and tinea pedis (Fig. 1A). The patient reported a history of frequent bacterial infections of the feet, as well as endometriosis, adenomyosis, and Ehlers-Danlos Syndrome. In the initial stages of the condition, the patient reported some thickening and yellowing of the nails, but with primarily normal growth. After prolonged infection, onycholysis developed, leading to nail ridging and detachment of the nail plate from the nail bed, with recurrent shedding. At the time of examination, the infection was limited to the right foot, but the patient had previously described the exact etiology on the left foot and other toes of the right foot. Beyond the toenail infection, the patient's feet showed signs of tinea pedis with cracking and peeling skin. No signs of fungal infection were found in the fingernails. Since the initial infection, the patient was prescribed various antifungal treatments without resolution (Table 1). Additionally, an oral fluconazole course was discontinued due to elevated liver enzymes and the development of frequent nausea. No attempts were made by physicians to identify or isolate the causative pathogen. The patient approached the researcher at the University of Idaho seeking to identify the fungal pathogen and develop a more effective treatment plan.

3. Isolation, colony characteristics, and cellular morphology of fungi associated with infected nail

Toenails were removed from the patient's right foot using sterile forceps. To prepare the toenail samples for direct microscopic examination, they were incubated for 1 minute with a 10 % (w/v) potassium hydroxide solution and mixed with a 5 mM calcofluor white solution. Septate fungal hyphae (~2 μm in diameter) with no observable branching were observed in toenail samples (Fig. 1B). Nail samples were also suspended in sterile phosphate-buffered saline (pH 7.0), mixed by vigorous vortexing, and the resulting solution was applied to yeast extract, peptone, and dextrose (YPD) agar with (15 μg mL^{-1}) chloramphenicol. Inoculated agar plates were incubated at 25 °C for up to 14 days.

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https://doi.org/10.1016/j.mmcr.2025.100715
Received 27 March 2025; Received in revised form 18 June 2025; Accepted 20 June 2025
Available online 21 June 2025