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Curvularia lunata-induced onychomycosis in an unlikely host

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Abstract

Onychomycosis, a fungal infection of the nail apparatus, presents varied manifestations, including subungual hyperkeratosis, onycholysis and nail plate destruction. Established risk factors include trauma, advanced age, and comorbidities like diabetes and immunosuppression [1]. Trichophyton rubrum, classified as a dermatophyte, is the primary causative agent, with overall dermatophytes contributing to 60-70% of cases. Non Dermatophyte Molds (NDM) account for 30-40% of onychomycosis with Candida species being the most commonly identified, while Curvularia species are rarely encountered [2]. This case report details a male patient in his fifties, presenting with xanthonychia, revealing a Curvularia lunata-induced onychomycosis through positive KOH preparation and culture. The patient's concurrent ticagrelor use necessitated a unique therapeutic approach with oral Terbinafine, resulting in complete resolution. The discussion emphasizes distinctions in disease severity among immunocompromised and immunocompetent patients, the potential role of trauma in Curvularia infections, and the importance of comprehensive diagnostic examinations.

Background

Onychomycosis is a fungal disease of the nail apparatus. It can present with various manifestations such as subungual hyperkeratosis, onycholysis, and nail plate destruction [3]. Established risk factors for onychomycosis include trauma, advanced age, and a history of tinea pedis [2]. Additionally, comorbidities like diabetes, obesity, immunosuppression, and malignancies are associated with increased risk. Onychomycosis can be caused by various fungi including dermatophytes, yeasts and nondermatophyte molds NDM [4]. The prevalence of onychomycosis varies due to several influencing factors. Generally, dermatophyte infections, also referred to as tinea unguium, are the most common, representing 60 to 70 percent. In contrast, nondermatophyte molds contribute 30 to 40 percent, and yeast infections account for 10 to 20 percent [2]. Trichophyton rubrum is the predominant dermatophyte in onychomycosis, constituting approximately 45 percent of infections [2]. Other dermatophytes implicated include Trichophyton mentagrophytes, Epidermophyton floccosum, Microsporum species, and other Trichophyton species. While the yeasts most frequently isolated from onychomycosis are Candida species. As for the molds, a variety of them have been isolated from nails [5]. According to Ramani R et al. (1993) study results, a 22% culture positivity rate for molds in onychomycosis cases was found. Notably, the predominant mold isolates comprised Aspergillus species (86.4%), Fusarium oxysporum (4.5%), Curvularia species (4.5%), and Penicillium species (4.5%).

The most prevalent presentation of fungal nail infection is distolateral subungual onychomycosis. Toenails are more commonly affected than fingernails. The fungus invades the nail and nail bed by penetrating the distal or lateral margins. The affected nail thickens and discolors, with different degrees of onycholysis. Invasion through the proximal margin, which is embedded within the proximal nail fold, is more prevalent in those with immunodeficiency (proximal subungual onychomycosis) [6]. Progression of the disease can lead to variants and overlap of these presentations.

Curvularia lunata is a saprobic dematiaceous mold that resides primarily in soil [1]. They spread via airborne spores and are a common cause of disease in plants. Curvularia can be microscopically distinguished from other dematiaceous fungi due to the presence of curved conidia [7]. The first reported human case was in 1959 as a corneal infection. Of approximately 40 recognized species, the most common causing human infection is Curvularia lunata [7]. Reports of human disease caused by this organism are rare but include endocarditis, brain abscess, skin infections, onychomycosis, keratitis, pneumonia, disseminated disease, mycetoma, allergic bronchopulmonary disease, and one case of sinusitisx [1].

Case presentation

The patient is a man in his fifties with a one-year history of xanthonychia, manifesting as discoloration in the distolateral aspect of his left big toenail (Figure 1). He mentioned a history of minor trauma, but there is no record of diabetes mellitus or any other predisposing factors. The patient's medical history revealed a background of dyslipidemia and coronary artery disease, which necessitated stent placement in 2020. Ongoing management involved the regular administration of rosuvastatin, aspirin, and ticagrelor. Prior to the consultation, the patient had not received any topical or systemic treatments for the nail discoloration. During physical examination, whitish-yellow discoloration was observed on the distolateral portion of the left big toenail. The other toenails were normal. In response to the clinical presentation, KOH preparation of nail scrapings was done and was positive for fungal elements. Scrapings stained with Giemsa revealed abundant septate, darkly pigmented hyphae. A nail culture was promptly ordered. The results of the culture confirmed the presence of Curvularia lunata, indicating a fungal etiology for the observed xanthonychia. Due to the opportunistic nature of the identified infection, a laboratory examination was conducted to assess for underlying immunosuppression, and the results returned negative. The standard therapeutic approach for Curvularia onychomycosis usually involves either oral itraconazole or oral terbinafine [9]. However, due to the identified interaction between oral itraconazole and ticagrelor (categorized as Risk Rating X with a recommendation to avoid concurrent use), the patient was prescribed a daily 250 mg oral terbinafine for a six-month duration, leading to complete resolution of the lesion (as depicted in Figure 2). This case is reported due to rarity of onychomycosis caused by curvularia in immunocompetent individuals.

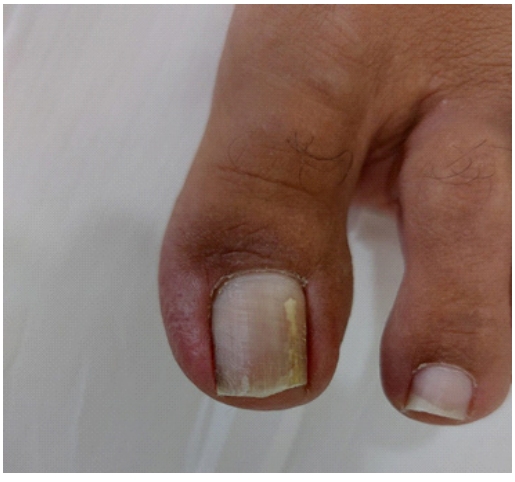

Figure 1: Showing clinical symptoms of diseased toenail.

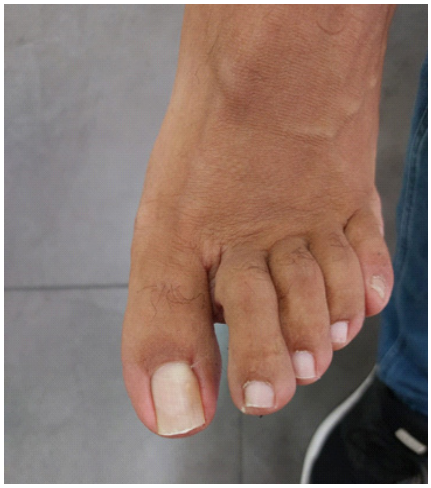

Figure 2: Complete resolution of the discoloration after six months of daily treatment with 250 mg of oral Terbinafine.

Discussion

Various studies have shown that the incidence of onychomycosis due to NDM has recently increased [8]. Curvularia species are ubiquitous, they reside primarily in soil and occasionally lead to infections in humans. Notable distinctions in presentation and severity of Curvularia infections are evident when comparing immunocompromised and immunocompetent patients. Immunocompromised individuals exhibited a more pronounced susceptibility to Curvularia, often presenting with more aggressive and disseminated forms of the infection encompassing conditions such as sinusitis, keratitis, pneumonia, mycetoma, allergic bronchopulmonary disease, endocarditis, brain abscess and disseminated disease [1]. In contrast, immunocompetent patients typically experience localized and less severe manifestations of Curvularia infections, often limited to conditions like onychomycosis [8].

Curvularia molds exhibit deep pigmentation owing to melanin in their hyphae and conidia, a characteristic that contributes to their pathogenicity [5]. The species causing human infections include Curvularia lunata, Curvularia pallescens, and Curvularia geniculata. Transmission occurs through inhalation or inoculation often triggered by factors such as perspiration, trauma, and exposure to soil saprophytes [8]. Cutaneous infections attributed to Curvularia tend to favor the extremities, often following a traumatic inoculation. Notably, toenail trauma has the potential to cause disruptions in the nail structure, creating entry points for fungal pathogens, including Curvularia. This can result in Curvularia-induced onychomycosis, even in immunocompetent individuals, providing a plausible explanation for the occurrence in our patient. Therefore, it is crucial to conduct a thorough history, including inquiries about occupation, recreational activities, or any routine that may be linked to the mode of transmission.

During the physical examination, patients often exhibit nail dystrophy suspicious of onychomycosis, such as discoloration, thickening, splitting, and nail plate destruction. As with any suspected onychomycosis, an accurate diagnosis involves both physical and microscopic examinations, along with culture [6]. The preferred initial test for suspected onychomycosis is a KOH preparation due to its rapid availability, relatively low cost, and procedural simplicity. Additionally, a nail clipping can be obtained for histopathologic examination using a PAS stain [2]. In the event of a positive KOH preparation or PAS stain confirming onychomycosis, we typically proceed to obtain a nail sample for fungal culture. This culture helps identify the causative organism, distinguishing between dermatophytes, yeast, and nondermatophyte molds, guiding subsequent treatment.

The scarcity of properly conducted paraclinical examinations, such as fungal cultures for onychomycosis cases, may

partially explain the infrequent detection of specific organisms. When diagnostic methods, such as cultures, are not routinely performed or are inadequately implemented, certain fungal organisms may go unnoticed. This lack of comprehensive testing can lead to underreporting and contribute to the perceived rarity of onychomycosis caused by certain fungal species, including Curvularia. In essence, the rarity might be attributed, at least in part, to the limitations in diagnostic practices, highlighting the importance of utilizing comprehensive paraclinical exams for a more accurate understanding of the prevalence and causative agents in onychomycosis cases.

Accurate identification of the causative agents in onychomycosis is essential for effective treatment, especially in light of potential antifungal resistance. Current treatment options for dematiaceous fungi infections like Curvularia induced onychomycosis include azoles (such as voriconazole, itraconazole), amphotericin B, terbinafine, and echinocandins [10]. Nevertheless, determining the most effective antifungal therapy remains uncertain. Consequently, physicians would carefully weigh factors such as infection severity, overall health, potential medication side effects, and drug–drug interactions to formulate a tailored management plan for each patient based on his personal factors. Topical antifungals like terbinafine or ciclopirox are often recommended for mild cases, applied directly to the affected toenail. However, the complexities of topical treatment, including limited access to the nail bed and pharmacologic properties required for nail plate penetration, pose challenges. Nail lacquers, such as ciclopirox 8%, amorolfine 5%, and efinaconazole 10%, are among the recommended options due to their unique pharmacologic properties, allowing for enhanced drug diffusion across the nail plate [11].

In severe cases, oral antifungal medications like terbinafine and itraconazole may be prescribed, although their usage demands caution due to associated risks. Terbinafine has been linked to hepatic injury, necessitating liver function tests [12], while itraconazole carries a high risk of drug interactions and should be approached cautiously in patients with cardiac conditions [13]. Fluconazole, another oral antifungal, presents cardiovascular risks and may prolong the QT interval [14].

Regarding nail debridement, which includes the trimming and removal of the infected nail portion, it can improve the efficacy of topical treatments [15]. It is imperative to adhere diligently to the prescribed treatment regimen, as the management of onychomycosis often demands patience and consistency. Furthermore, preventing reinfection through the practice of good foot hygiene, maintaining dry feet, and avoiding environments conducive to fungal growth is crucial. Regular follow-ups with a healthcare professional are advisable to monitor progress and make any necessary adjustments to the treatment plan.

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