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Onychomycosis

Diagnosis, Treatment, and Prevention

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ABSTRACT

Toenail disorders account for the majority of foot complaints for which adults seek medical care. Onychomycosis, a fungal nail infection, is the most prevalent. Dermatophytes are responsible for the majority of nail infections and cause varying degrees of nail deformities. While several treatment strategies are available, no one approach (topical, systemic, or mechanical) is highly curative. This article reviews causes, diagnosis, and treatment options for onychomycosis and provides patient education tips to prevent and limit the spread of the disease.

KEY WORDS: Dermatophytes, Nail deformities, Nail fungal infection, Onychomycosis.

INTRODUCTION

Toenail disorders are one of the most prevalent foot complaints for which adults seek over-the-counter treatments and professional care, especially for recalcitrant fungal infections. Onychomycosis or fungal disease of the nails is the most widespread nail disorder affecting 3% of the general adult population worldwide.[1] While the exact number of individuals per age group is unavailable due to the lack of large-scale prevalence studies, it is estimated that 20% of individuals between the ages of 40 and 60 years are affected.[2] Onychomycosis is prevalent in older adults, affecting 50% of those older than 70 years; the condition rarely affects children.[2]

Causative factors vary by geography, race, and ethnicity; however, dermatophytes account for approximately 90% of all toenail infections.[3] The most common dermatophytes affecting the toenails include *Trichophyton rubrum and Trichophyton interdigitale*, while saprophytes, *Candida*, and molds are responsible for about 5% of infections.[3] Other factors include nail trauma, occlusive footwear, chronically moist feet, hyperhidrosis, comorbid conditions such as HIV infection, psoriasis, and peripheral vascular disease, and genetic predisposition. Immunosuppression is also a well-established factor, placing individuals at risk for toenail infection. Fungal nail disease occurs more frequently in males and affects approximately 34% of individuals with diabetes mellitus.[3] Concomitant dermatophytosis of the skin and nails affects about one-third of individuals with fungal infections.

Quality of life can be substantially reduced by onychomycosis. Unfortunately, fungal infections are often considered a problem of cosmesis and patients may defer treatment until there is extensive nail involvement, rendering eradication time-consuming and costly.[4] Embarrassment of having thick discolored nails, discomfort with wearing shoes and walking, and lowered self-esteem are notable problems. Some patients report severely dystrophic toenails that negatively influence their sexual activity and intimate relationships. In addition, damage to shoes, socks, and stockings due to the constant friction with sharp and thick nails is frustrating for patients. Finally, there is a misconception that onychomycosis is not contagious, even though research indicates that it is easily spread to family members if left untreated.[5]

The clinical manifestations of fungal nail disease vary according to the level of invasion of the 3 layers of the nail plate and the underlying nail bed. The fungus enters the distal or lateral nail margins and then invades the nail and the nail bed, leading to dystrophy and discoloration. As the condition progresses, the nail plate may separate from the bed. Depending on the organism, the plate may become thin and brittle or, conversely, excessively thick and crumbly. The patterns of nail involvement are classified as superficial white in which the top outer layer of the nail has small white opaque friable patches that are easily scraped away; distal subungal, the most common presentation in which the middle layer hypertrophies and distorts the nail; and less common proximal subungal infection in which white fungal elements are seen under the proximal nail plate. The infection is initially confined to one side of the nail but spreads rapidly to produce gross white discoloration and thickening of the entire nail plate.

Another common nail condition that involves the nail plate is subungal hyperkeratosis, characterized by an accumulation of scales under the nail plate that cause the nail to detach and "lift up" from the nail bed. Caused by an excessive proliferation of nail bed keratinocytes, the condition is most commonly associated with psoriasis, contact dermatitis, and subungal onychomycosis. Many noninfectious conditions produce nail dystrophy that may resemble a fungal infection; however, they have different characteristics. For example, a subungual malignant melanoma may present as a small discolored "dot," whereas subungual trauma often has a characteristic red "bruised" appearance during the acute stage and becomes dark purplish as the blood under the nail dries when it becomes chronic. Nails affected by lichen planus are often dark. Trauma-induced nail dystrophy can be twice as common as onychomycosis.

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Diagnosing a fungal infection is often difficult based on clinical signs alone.[6] As noted previously, there are a number of other infections or conditions that mimic onychomycosis such as *Candida* and bacterial infections. Candida infection or candidosis usually begins in the proximal nail plate and is accompanied by infection of the nail fold (paronychia)—the skin around the nail appears red and inflamed. Bacterial infections from organisms such as *Pseudomonas aeruginosa* can present as a green or black nail discoloration and create an odor. Clinicians should be aware that fungal and bacterial infections may coexist.

Laboratory studies should be conducted prior to starting treatment.[7] The goal of this evaluation is to rule out nonfungal conditions, detect mixed infections, and determine the type of fungal etiology needed to guide the most effective treatment. Obtaining a good nail specimen can be tricky but is necessary to ensure accuracy in the diagnostic confirmation. Use of a curette, scalpel, or other sharp device is recommended to obtain affected nail material. Any discolored, loosened, thickened, crumbly, or brittle parts of the nail should be included in the specimen.

Culture and microscopy are the traditional methods to analyze the nail specimens.[7] Newer methods using molecular genetic techniques have been implemented such as real-time polymerase chain reaction (PCR) assays to detect dermatophytes and offer a very rapid turnaround time of a few days. One limitation of PCR analysis is that it also detects nonpathogenic or inactive fungal elements, which may reduce its utility in the identification of the actual pathogen.

New evidence suggests that onychomycosis prognosis may be linked to pathogens manipulating host immune responses, making some individuals with specific genetic mutations more susceptible to onychomycosis infection.[7] Aggressive treatment of onychomycosis prior to symptom progression is most beneficial for these individuals. Treatment strategies are most effective when started early, but management is often delayed when the patient defers seeking evaluation until the infection has progressed to the point that it causes discomfort. Patients with onychomycosis and concurrent peripheral neuropathy also tend to delay treatment because perceptions of pain/discomfort are blunted or absent.

SYSTEMIC PHARMACOTHERAPY

Multiple interventions are effective for the various pathogens associated with onychomycosis. Optimal management of dystrophic toenails related to fungal infection is based on knowledge of clinical versus mycologic cure rates.[7] A clinical cure is defined as a normal appearance of the nail and the absence of clinical signs such as subungal hyperkerotosis, nail discoloration, and nail plate thickening. Mycologic cure is based on microscopy or a negative nail culture. Negative culture may be accompanied by clinical signs of infection such as minimal distal subungal hyperkeratosis and nail plate thickening. We recommend educating patients that nails take a year or more to grow out and may be improved but not perfect in appearance. Although nail appearance will usually continue to improve after cessation of therapy, the nails may have a persistent abnormal appearance even in cases where treatment has been effective. There is also a high recurrence rate following treatment.

Two main oral systemic therapies have emerged as the most effective against onychomycosis.[8,9,10] Terbinafine is associated with higher clinical cure rates and mycological cure rates when compared to azole medications such as itraconazole, though both are considered first-line treatments of onychomycosis. Clinical cure rates for both drugs range from 31% to 57% and mycological cure rates from 43% to 76%. Unfortunately, treatment failure is common (24%-69%). The majority of treatment studies were conducted in otherwise healthy volunteers. Individuals with diabetes or peripheral vascular disease, common comorbid conditions, were not included in the efficacy studies for treatment of onychomycosis.

Terbinafine is typically prescribed as 250 mg daily for 12 weeks or 500 mg once daily for 1 week each month for 3 months. There are relatively few significant drug interactions. However, as a CYP2D6 inhibitor, it can increase systemic levels of certain β-blockers, antidepressants, and antiarrhythmic agents. Liver function should be checked at baseline; terbinafine is not recommended for individuals with liver disease.

Itraconazole is prescribed for onychomycosis as 200 mg daily for 12 weeks or 200 mg for 1 week each month for 3 months. Itraconazole is a CYP3A4 substrate and inhibitor that may cause drug-drug interactions when administered with lovastatin, simvastatin, triazolam, quinidine, pimozide, methadone, and several other drugs. It is contraindicated in patients taking these drugs.

It can also cause increased levels of carbamazepine, calcium channel blockers, and digoxin. The United States Food and Drug Administration (US FDA) has issued a Boxed warning that itraconazole can worsen heart failure and is not recommended in patients with liver disease. Baseline liver function should be checked in addition to periodic monitoring due to the risk of hepatotoxicity. We have observed that itraconazole is recommended less often because of these risks and interactions.

TOPICAL PHARMACOTHERAPY

Topical agents have been developed to treat onychomycosis due, in part, to the number and severity of adverse effects associated with systemic therapy.[11-13] Unfortunately, topical agents such as nail lagers/paints and ointments have suboptimal efficacy. They can be considered for patients who cannot or will not use oral therapy or individuals with superficial white onychomycosis or infection only of the nail tip. Topical prescription agents should be applied directly to the nail daily for 48 weeks and have cure rates that range from 7% to 27%. Medications in this category include ciclopirox, efinaconazole, tavaborole, and propylene glycol/urea/lactic acid preparations. Topical antifungals struggle to penetrate the nail plate at fungicidal concentrations and may require debridement of the nail plate prior to application.

Several nonprescription options to treat onychomycosis have been described anecdotally in the lay literature; very few studies are noted in the scientific literature. The lack of effectiveness of topical prescription medications to treat onychomycosis continues to make treatments such as mentholated ointment, essential oils such as tea tree, clove, thyme, eucalyptus, lavender, and oregano, and vinegar popular; however, there is insufficient evidence to recommend these treatments.[11-13]

LASER

With systemic and topical antifungals showing limited effectiveness, laser (light amplification by stimulated emission of radiation) has emerged as a treatment option approved by the US FDA.[14] Pulsed laser treatment causes accumulation of heat within the nail, creating a fungicidal effect and alleviating pain and necrosis in the surrounding tissues. Unfortunately, this limits the effectiveness of the laser therapy.

The US FDA recommends that lasers should be evaluated using aesthetic endpoints such as amount of clear nail as

opposed to medical endpoints (eg, mycological cure, complete cure). Laser studies provide preliminary evidence of clinical improvement and clear nail growth in toenail onychomycosis with temporary improvement in less than 50% of patients. Laser therapy is not considered a first-line treatment option because it has not shown efficacy rates that exceed or equate those found with oral and topical treatments.

MECHANICAL DEBRIDEMENT

Mechanical debridement has been shown to enhance efficacy when combined with other interventions.[15] Reducing nail thickness with the use of nail nippers and/or rotary files designed for toenails decreases the mycologic burden of the nail, provides immediate relief from discomfort, and improves the nail's appearance. In addition, topical solutions can better penetrate the nail following debridement, allowing access to the nail bed where fungal proliferation occurs.

Nevertheless, mechanical debridement provides only temporary relief; the nail will continue to grow, requiring repeated debridement to continue to be effective. Many individuals with onychomycosis are unable to perform their own nail care and will need assistance for daily application of a topical agent. When faced with the long duration of treatment for topical therapies and the potential of side effects or drug interactions from oral therapies, many individuals opt for mechanical debridement to manage their thick, mycotic nails. Mechanical debridement is also an effective management strategy for other nail dystrophies. It is essential that appropriate infection prevention strategies are applied when using mechanical debridement. For example, equipment must be cleaned and sterilized to prevent the spread of infection and the person administering mechanical debridement should wear protective masks and clothing.

CONCLUSION

Prevention remains the most effective way to prevent onychomycosis; treatment failure occurs in 25% to 40% of patients with onychomycosis due to lack of adherence to prescribed treatments, and poor drug selection, penetration, and resistance remain. In addition, onychomycosis recurs in 40% to 70% of cases. Dermatophytes are found in many hotel rooms, showers, flooring, and public areas such as gyms, and patients should be instructed to wear footwear such as antifungal/microbial slippers or flip-flops to reduce exposure. Alternatively, patients can be counseled to sprinkle absorbent and antifungal powders containing tolnaftate, clotrimazole, or miconazole to prevent infection. Wearing synthetic socks that wick away moisture is also advised. Sharing toenail clippers and files should be avoided. Finally, discarding older footwear and wearing well-fitting shoes and new socks/stockings aid in reducing exposure to fungal elements. When your patient asks about manicures and pedicures, instruct them to find salons that use sterile instruments. Individuals should also keep their own clippers and files clean by putting them in the dishwasher after every use.

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