Making strides in preventing onychomycosis recurrence
Melodie S. Young, David M. Pariser, Phoebe Rich and Nathaniel J. Jellinek
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Abstract:

Onychomycosis is a clinically important infection that is frequently progressive and may be associated with clinical sequelae. Accurate diagnosis, appropriate choice of antifungal agent--with consideration given to particular patient characteristics, including the presence of concomitant diseases and ability to comply with a given regimen--careful follow-up, and consideration of long-term management and reinfection prevention strategies are crucial to successful treatment.

Keywords

Onychomycosis

Full Text:

Onychomycosis is an important medical condition that warrants clinical intervention. (1) Untreated or undertreated, onychomycosis often is progressive and is associated with a number of possible clinical sequelae. In addition, this contagious infectious disease can be transmitted to others via direct contact or on surfaces such as shoes, patios surrounding pools or spas, or showers and bathtubs. Fungal infection in the toenails also may spread from the feet to other areas of the body.

In individuals with comorbidities, onychomycosis can lead to complications. In select circumstances (such as for patients with immunosuppression or diabetes), thick onychomycotic nails may traumatize adjacent skin, leading to secondary bacterial infections that may develop and can result in cellulitis and ulcerations. (1,2) Permanent damage may occur to the nail plate and its attachments, possibly leading to interference with normal gait. This, in turn, may increase the associated risk for falls in older patients. Finally, onychomycosis may adversely affect overall quality of life, including embarrassment, self-consciousness, and interference with relationships when patients fear transmitting the infection to others. (3-4)

Patients who seek medical attention for onychomycosis do so because of a variety of signs or symptoms that they find bothersome, which include pain and discomfort in the affected toenail, a history of nail shedding, concern that the infection will spread to other nails or other parts of the body, the presence of a secondary infection of the skin surrounding the nail plate, unsightly appearance, or interference with a patient's ability to walk normally.

In contrast, patients with mild onychomycosis in one or two toes may be less bothered either by symptoms or the appearance of the nails and less likely to request evaluation and management of nail changes during a visit with the clinician. Even those with long-standing infections and moderate to severe signs of onychomycosis (such as yellowing, brittleness, and lifting of the nail plate) may not mention such changes. Thus, the presence of onychomycosis may come to the attention of the clinician only as an incidental finding during a clinical encounter for some other purpose, such as an annual full-body dermatologic skin examination and careful inspection of unpainted nails.

When a clinician notes the likely presence of fungal infection as an incidental finding, some patients express no interest in pursuing further diagnostic measures (to confirm the diagnosis and identify the causative organism) or treatment. This is especially true when the disease is mild and not symptomatically or cosmetically bothersome, but sometimes patients with more severe disease decline a clinician's offer to "do something about your toenail fungus." It is important for clinicians to understand and communicate the rationale for definitive medical treatment of onychomycosis and the availability of recently improved options for therapy.

Treatment Goals

Ideally, treatment should result in both mycologic and clinical cure--or complete cure. Mycologic cure is
defined as a negative result on potassium hydroxide (KOH) preparation and the absence of organisms on fungal culture and/or periodic acid-Schiff (PAS) staining on pathologic analysis. Clinical cure is the completely normal appearance of the nail. In clinical trials, complete cure is used as the primary end point to determine efficacy.

In the clinical setting, the rigorous standard of complete cure is not always achieved and cannot always be expected. In many cases, particularly when patients have not been treated previously for onychomycosis, a negative result on KOH examination may be acceptable evidence of mycologic cure, without the need for the additional step of obtaining a fungal culture, if the affected nails show complete clinical clearance—that is, the previously infected nail plate has grown out and been replaced with a normal-appearing nail. Although resolution of the infection in patients who are treated early and effectively may result in a completely normal-appearing nail, individuals with long-standing infections or recurrent onychomycosis may have sustained permanent damage to the nail matrix or subungual tissue. In the latter group, mycologic cure may be achieved but the nails may still appear discolored or dystrophic and onycholysis (lifting of the nail plate) may persist. Furthermore, some patients have thickened, discolored, or dystrophic nails for reasons unrelated to nail infection—for example, changes related to chronic microtrauma, aging, or concomitant psoriatic nail disease. For those patients, achieving complete cure is much more difficult or, in some cases, impossible.

These concepts of cure must be considered and applied to individual patients, and expectations for treatment outcomes should be carefully explained to patients before therapy is initiated.

Onychomycosis Persistence and Recurrence

Onychomycosis has a high relapse rate after successful therapy, so successful eradication of signs and symptoms represents only the first step in management. Clinicians and patients must understand that adherence to initial treatment and follow-up—as well as attention to measures that reduce the risk for recurrence, and, when necessary, retreatment—all optimize the chances for long-term control of onychomycosis.

Onychomycosis is a chronic problem for as many as 25% of patients seen in clinical practice (5) and may persist or recur for any of several reasons. In many cases, the risk for recurrence is modifiable. Perhaps the most common—and most readily avoidable—reason for lack of treatment efficacy is inaccurate diagnosis. Although onychomycosis is the most common nail disease, several nonfungal causes of nail symptoms that may mimic onychomycosis must be considered in the differential diagnosis in adults (Table 1). (6-8) These causes are multiple and include psoriasis, lichen planus and other immune-mediated inflammatory diseases, chronic microtrauma or macrotoma, and local tumors. Thus, clinical inspection is not sufficient for a diagnosis of onychomycosis; some objective test is required for a definitive diagnosis. A KOH preparation can be done to detect the presence of fungal organisms; if no fungi are detected, nonfungal or noninfectious causes for symptoms should be considered. A nail specimen can be obtained for culture to determine whether nonfungal organisms are present or infections are mixed, including both dermatophyte organisms and nondermatophyte molds or yeast. Identification of the infecting organisms can substantially affect treatment choices and prognosis. Sampling of the nail plate and bed debris for pathologic analysis (and PAS staining) is considered by many to be the most sensitive and specific test, although it lacks specificity in identifying organism species. Often clinicians will perform several of these tests to achieve the most accurate diagnosis.

Another important modifiable cause for treatment failure or infection recurrence is poor adherence to treatment. Patients must understand that even if the onychomycosis treatment they are using is maximally effective, the results will not be apparent until the nail grows out in the absence of fungal organisms and associated trauma and/or inflammation. Because toenails grow at the rate of approximately 1 mm per month—and more slowly in older individuals—an effectively treated nail may not appear completely normal for 12 to 18 months.

Recurrence also is associated with tinea pedis; the latter infection often is caused by the dermatophyte T. rubrum, the most common causative organism in onychomycosis. Thus, one important strategy for preventing recurrence of onychomycosis is preventing, monitoring for, and effectively treating tinea pedis.

Topical medication for hyperkeratotic (moccasin-type) infection should be applied to the bottoms and sides of the feet. Patients with interdigital infection should be instructed to apply topical medication to these areas as
well as to the soles of the feet. Recurrence of tinea pedis often is due to a patient's discontinuance of medication after symptoms resolve; thus, patient education about the importance of controlling the fungal carriage on the feet is crucial to adherence to a treatment regimen.

Guiding Patient Expectations

Clinicians are in an ideal position to discuss treatment options, noting that systemic and topical agents are available, and to clearly explain the reason for recommending either type of approach and specific agent(s) in the particular patient's case. Patients should be advised about any potential adverse effects associated with the recommended therapy and about the expected cure rates. If systemic therapy is considered, the patient should be informed about any baseline and/or monitoring tests (such as liver function tests) that will be required.

As noted previously, many patients will not experience completely normal nail growth, despite the improved appearance of the nail. At the very least, most patients can expect mycologic improvement, if not complete cure. Several factors have been identified as indicators of a poor prognosis for a complete cure in adults (5-9) (Table 2), including a greater than 50% area of nail involvement, significant lateral disease, subungual hyperkeratosis (greater than 2 mm), the appearance of white/yellow or orange/brown streaks in the nail, the presence of dermatophytoma, total dystrophic onychomycosis with matrix involvement, or infection with nondermatophyte molds. In addition, complete cures may be less likely in patients who are immunocompromised or who have compromised peripheral circulation.

Promoting Treatment Adherence

Because adherence is such an important modifiable factor in the recurrence of onychomycosis, special attention should be paid to strategies for improving the proper and consistent use of medications. Clinicians typically encounter two major underlying causes for lack of adherence in patients with onychomycosis: patient perception that the medication is not working fast enough (ie, the growth of normal nail is not recognized) and patient perception that the medication is not working well enough (ie, the changes in the nail are seen by the patient as an improvement, but the patient does not judge the new growth to appear "normal"). Both issues should be addressed at the time of diagnosis and prior to the initiation of therapy as well as during follow-up visits.

Patients must be told that toenails grow slowly, at the rate of approximately 1 mm per month. A visual reference may be helpful, such as showing the patient the side of a US nickel and noting that it is 1.95 mm thick. Even if the medication eliminated all active fungal organisms on the first day of treatment, the amount of normal nail that could be seen after 1 month would be about one half to a full thickness of a nickel. Therefore, it is difficult to judge the effectiveness of a treatment that is used correctly and consistently until after at least 3 to 4 months of treatment, and a completely "new" nail should not be expected for 12 to 18 months (longer in older individuals whose nails grow more slowly than in younger individuals).

Although dermatologists routinely document skin and nail conditions photographically at diagnosis and during follow-up visits, these photos are maintained in patient files. As most patients have cell phones with cameras, one way to overcome the hurdle of delayed treatment gratification and provide encouragement for persistence with onychomycosis therapy is for patients to use their cell phones to take a clinical photograph prior to the start of treatment and then take a new photograph each month so that the clinician and the patient can review the pictures together at the next follow-up visit.

Finally, incorporating antifungal treatment—whether systemic or topical—into the daily grooming routine can be one way to promote adherence, including storing the medication in a place where it is most likely to be accessible for dosing or application. For example, systemic antifungal agents might be kept on a kitchen shelf with other medications or supplements that already are part of a patient's daily routine. Topical medications might be stored in the bathroom, readily at hand for application right after a daily shower, or on the bedside table near the chair the patient sits in to put on socks and shoes.

Patient-Focused Strategies for Preventing Recurrence

Patients must appreciate that fungi are ubiquitous and that nearly everyone comes into contact with these organisms. However, some individuals seem to have a natural immunity for fungal infections despite regular
contact with dermatophytes, and others acquire a fungal infection once or twice in a lifetime. Other individuals are so prone to infections and reinfections that they develop a pattern of repeated involvement over a period of time or even a lifetime. Clinicians must be clear with patients that onychomycosis tends to recur and, for some patients, episodic treatment will be necessary to manage recurrent infections. Strategies exist that may help reduce an individual's risk for infection recurrence. The more thoroughly patients understand the nature of onychomycosis, the more likely they will be to implement these recurrence-reducing measures and to seek treatment when they experience recurrences.

Patients must recognize that onychomycosis is an infectious disease that is caused, in most cases, by dermatophyte fungal species. It is acquired from some source, and often is reacquired from the same or similar sources. Onychomycosis infection is unrelated specifically to hygiene; it is related to individual susceptibility. However, even susceptible individuals can take measures to limit their exposure to sources of fungal infections and to enhance their ability to resist recurrence of onychomycosis (Table 3 on page 18).

Patients may ask about the possibility of "sanitizing" footwear to prevent reinfection. Several methods of decontamination have been investigated, but it is not clear whether elimination of fungal reserves from footwear is possible.

Conclusion

Research over the past two decades has led to advances in understanding the natural history and clinical importance of mycologic infections of the toenails. Onychomycosis frequently is a progressive infection and is associated with a number of clinical sequelae. This relatively recent recognition of the clinical importance of onychomycosis—as well as the availability of more effective antifungal medications, including newer topical agents—have contributed to the appreciation of this infectious disease as a treatable condition that warrants intervention. Successful treatment depends on an accurate diagnosis (see "Onychomycosis Diagnostic Techniques and the Office-Based Clinician" on page 16) and patient adherence to long-term therapy, as well as the recognition that recurrence is common and requires follow-up treatment. It is possible that a maintenance regimen of topical therapy may either prevent or reduce the number of recurrences of onychomycosis and its associated infection, tinea pedis. However, to date, no study has been conducted to determine the efficacy, safety, and feasibility of such a maintenance topical therapy strategy.

Onychomycosis Diagnostic Techniques and the Office-Based Clinician

Because of Clinical Laboratory Improvement Amendments certification requirements, many dermatologists no longer perform certain laboratory tests in office-based practices. However, no special training is required to perform a microscopic inspection of a specimen prepared with 10% to 15% potassium hydroxide. This method allows on-site and rapid confirmation of the presence of a fungal infection.

In patients with distal subungual onychomycosis, the nail should be debrided as far back as possible and a specimen of subungal debris should be scraped from an area as close to the cuticle as possible; scale from the nail plate also can be used. A sample from deeper under the nail plate and the nail bed is needed for proximal subungual onychomycosis. In patients with suspected superficial white onychomycosis, nail plate scrapings are preferred. Adding dimethyl sulfoxide on the slide will help dissolve debris and facilitate visualization of the fungus; the use of chlorazol black E or Parker blue-black ink will enhance visualization, if necessary.

A more sensitive method of diagnosis is histologic examination of periodic-acid Schiff stained preparations of nail plate and subungual tissue specimens, performed by a dermatopathology laboratory. The disadvantages of this test are the lack of immediacy (results usually are available in a few days), the possibility that results may not be conclusive (the presence of septate hyphae is diagnostic, but the presence of yeast forms alone is not definitive), and the inability to identify specific organisms and species.

Fungal culture is the only widely available method for establishing both the presence of infection and the causative organism. Although many laboratories perform mycology studies, only a few in the United States specialize in such cultures and can, on request, also test for drug sensitivity.

References


Melodie S. Young, MSN, RN, A/GNP-c, * David M. Pariser, MD, ([dagger]) Phoebe Rich, MD, ([double dagger]) and Nathaniel J. Jellinek, MD ([section])

* Modern Dermatology, a Baylor Health Texas Affiliate, Dallas, Texas

([dagger]) Professor of Dermatology, Eastern Virginia Medical School, Department of Dermatology, Pariser Dermatology, Norfolk, Virginia

([double dagger]) Clinical Adjunct Professor of Dermatology, Oregon Health Science University, Portland, Oregon

([section]) Assistant Clinical Professor, Department of Dermatology, Warren Alpert Medical School at Brown University, Adjunct Assistant Clinical Professor, Division of Dermatology, University of Massachusetts Medical School, Fellowship Director, Procedural Dermatology, Dermatology Professionals, Inc., East Greenwich, Rhode Island

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Address reprint requests to: Melodie S. Young, MSN, RN, A/GNP-c, Modern Dermatology--Aesthetics Center Dallas, 9101 N. Central Expressway, Suite 160, Dallas, TX 75231; melodieyoung@aol.com
TABLE 1. Differential Diagnosis of Onychomycosis in Adults

* Bacterial infection
* Chronic paronychia
* Contact irritants/dermatitis
* Lichen planus
* Nail trauma (eg, from ill-fitting footwear, injury during pedicure)
* Neoplasms (squamous cell carcinoma, fibroma, melanoma)
* Psoriasis
* Vascular conditions
* Verrucae of nail folds or subungual tissue

Sources: Allevato (6); Cockerell and Odom (7); Daniel (8)

TABLE 2. Indicators of a Poor Prognosis for Complete Cure of Onychomycosis

Nail-specific factors

* >50% area of nail involvement
* Significant lateral disease
* Subungual hyperkeratosis (>2 mm)
* White/yellow or orange/brown streaks in the nail
* Presence of dermatophytoma
* Total dystrophic onychomycosis with matrix involvement
* Infection with nondermatophyte molds

Patient-specific factors

* Immunocompromised host
* Compromised peripheral circulation

Sources: Scher and Baran (5); Scher et al (9)

TABLE 3. Common Sources of Reinfection With Organisms That Cause Onychomycosis

* Infected footwear
* Improperly fitting footwear

* Tinea pedis infection

* Exposure to other household members with tinea pedis

* Sharing nail clippers and files with an individual with onychomycosis

* Improper nail grooming

* Exposure to fungal organisms at nail salons (manicure/pedicure tools and soaking containers/tubs)

* Public facilities such as pools, spas, locker rooms, and gyms

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