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A REVIEW ON ONYCHOMYCOSIS

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ABSTRACT
Onychomycosis is the most common nail infective disorder. It is caused mainly by anthropophilic dermatophytes, in particular by Trichophyton rubrum and T. mentagrophytesvar. interdigitale. Yeasts, like Candida albicans and C. parapsilosis, and molds, likeAspergillus spp., represent the second cause of onychomycosis. The clinical suspect of onychomycosis should be confirmed my mycology. Onychoscopy is a new method that can help the physician, as in onychomycosis, it shows a typical fringed proximal margin. Treatment is chosen depending on the modality of nail invasion, fungus species and the number of affected nails. Oral treatments are often limited by drug interactions, while topical antifungal lacquers have less efficacy. A combination of both oral and systemic treatment is often the best choice.

Keywords: *onychomycosis; nail lacquers; systemic antifungal therapy; fungi; nail.*

INTRODUCTION
Onychomycosis is the most common nail infective disorder, and it is responsible for about 50% of all consultations for nail disorders. Onychomycosis has been reported as a gender- and age-related disease, being more prevalent in males and increasing with age in both genders. In the elderly, onychomycosis may have an incidence >40%. Predisposing factors are diabetes mellitus, peripheral arterial disease, immunosuppression due to HIV or immunosuppressive agents.

In most cases, this infection is caused by anthropophilic dermatophytes, in particular by Trichophyton rubrum, followed by Trichophyton mentagrophytes var. interdigitale. The non-dermatophyte molds, like Scopulariopsis brevicaulis and Aspergillus spp., can be involved in onychomycosis as primary pathogens or as contaminant agents and secondary pathogen. Other molds that have been isolated from affected nails include Fusarium spp., Acremonium spp., Alternaria spp. and Neoscytalidium sp. The estimated worldwide prevalence of non-dermatophyte molds onychomycosis is 10%–15%. Yeasts, like Candida albicans and Candida parapsilosis, represent the third cause of nail fungal infection, and they occur only when predisposing factors are present, mainly immunosuppression and diabetes

Toenails are more commonly affected than fingernails: onychomycosis in these cases frequently involves several nails, and dry-type plantar tinea pedis is often present. There are different clinical types of onychomycosis, depending on the modality of nail invasion. Clinical diagnosis of onychomycosis always requires laboratory confirmation, and treatment depends on many factors, like the fungus species and the number of affected nails.

Onychomycosis in childhood is rare and affects approximately 0.5% to 2.6% of all children. Similar to adults, the most common presentation is distal subungual onychomycosis, and toenails are affected more commonly than fingernails. Children acquire the fungus from a dystrophic or traumatic nail abnormality or from a parent, indirectly, through environment contamination. Genetic predisposition to develop fungal invasion of the soles and nails seems necessary at a young age.

Clinical Features

Distal and Lateral Subungual Onychomycosis

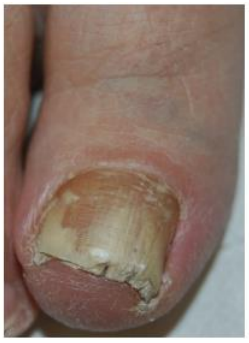

Figure 1. Distal and lateral subungual onychomycosis (DLSO): whitish discoloration, onycholysis and subungual hyperkeratosis.

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Through the hyponychium, fungi enter the nail and spread proximally on the surface of the nail unit plate. One or both of the great toenails are typically affected by distal and lateral subungual onychomycosis (DLSO), which is frequently accompanied with tinea pedis. The nail plate has a yellow-white appearance, is onycholytically separated, and has distal subungual hyperkeratosis. Less frequently, the onycholytic nail may develop a brown, black, or orange colour.

Dermatophytoma, a subungual accumulation of hyphae and scales that is hardly touched by antifungals and involves excision of the region and systemic treatment, is one potential dermatophyte-related DLSO presentation.

When the infection is the Melanoides form of Trichophyton rubrum or another fungus that produces melanin, such as Neoscytalidium dimidiatum or Aspergillus niger, DLSO may be accompanied by black nail pigmentation (also known as "fungal melanonychia"). Non-dermatophyte-caused onychomycosis is frequently accompanied by a severe periungual irritation.

Traumatic onycholysis (typically symmetrical and subungual hyperkeratosis is absent) and nail psoriasis (diffuse hyperkeratosis, multiple/all toenail involvement, additional skin and nail indications of psoriasis) are two alternative diagnosis for DLSO.

Superficial Onychomycosis in White

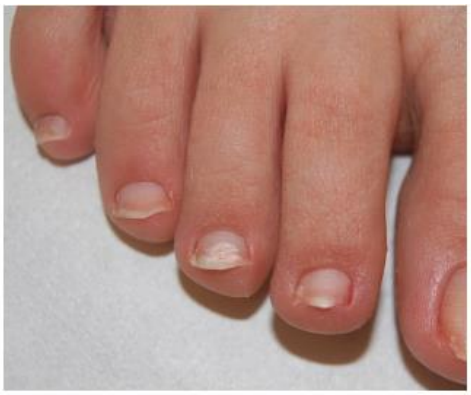

Figure 2. White superficial onychomycosis (WSO): white opaque friable patches of the nail plate.

Fungi colonise the dorsal nail plate, appearing as white, opaque structures that can be removed with a scraper. The classic form of this condition is caused by Trichophyton interdigitale, in which dermatophytes colonise the nail plate's outermost layers without actually penetrating it (Figure 5). However, Fusarium species and other moulds can also result in a condition called white superficial onychomycosis (WSO), which has a deeper nail invasion.

It is typical for T. interdigitale to cause tinea pedis interdigitalis (athlete's foot).

The differential diagnosis includes transverse toenail leukonychia from trauma and superficial nail fragility from prolonged nail polish usage.

Proximal Subungual Onychomycosis

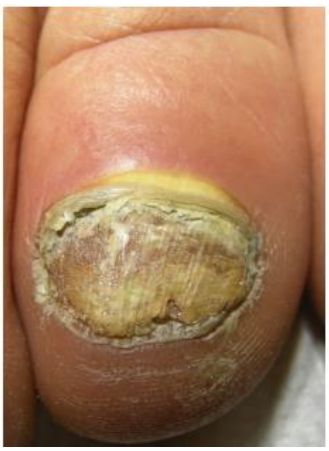

Figure 3. Proximal subungual onychomycosis (PSO): white discoloration of the proximal nail plate.

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Typically, fungus-related components are found in the ventral nail plate, resulting in proximal leukonychia. Proximal subungual onychomycosis (PSO) caused by dermatophytes is extremely uncommon, and the T. rubrum type was once thought to be an indication of HIV infection. It appears as a white spot in the lunula region, beneath the proximal nail plate. Acute periungual inflammation is frequently present with PSO, which is a common presentation of non-dermatophyte mould infection, particularly caused by Aspergillus sp. and Fusarium sp.Acute bacterial paronychia and pustular nail psoriasis are included in the differential diagnosis.

Endomycosis Endonyx

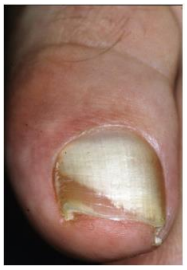

Figure 4. Endonyx onychomycosis: white discoloration of the nail plate that is firmly attached to the nail bed.

Massive nail plate invasion without nail bed involvement is the hallmark of endonyx onychomycosis. Clinically, the damaged nail may have milky white discolouration and lamellar cracking.

There is no onycholysis or nail bed hyperkeratosis, and the nail plate is firmly affixed to the nail bed.

It is very uncommon and brought on by T. soudanense or T. violaceum.

Onychomycosis with total dystrophy

The most serious stage of onychomycosis, total dystrophic onychomycosis (TDO), can arise from persistent DLSO or PSO. The nail plate is friable, yellowish, and has a widespread thickening.

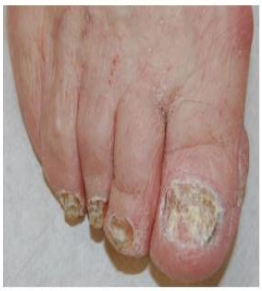

Figure 5. Total onychomycosis: the nail plate is completely invaded by fungi and friable

Onychomycosis diagnosis

Mycology should be used to confirm the clinical suspicion of onychomycosis. The mycological examination is divided into two parts: direct microscopic examination and culture. For the first, the nail material is collected from the affected nail and immersed in a 40% KOH solution before being placed on a slide and examined under an optical microscope for hyphae and spores. KOH does not identify the type of fungus causing onychomycosis, and a culture is required for a more specific diagnosis. Histopathology of nail clippings can be used to diagnose onychomycosis, with periodic acid-Schiff (PAS) stain allowing easy visualisation of fungal hyphae.

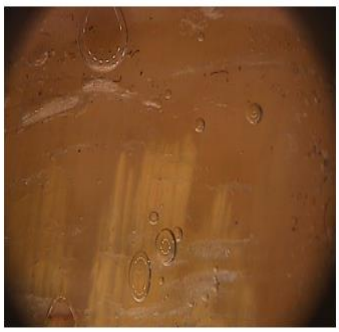

Figure 6. Onychoscopy of DLSO, showing the typical proximal fringed (ragged) margin.

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Digital dermoscopy, also known as onychoscopy, is a simple and quick procedure that allows for the differentiation of onychomycosis from common nail dystrophies.

The following DLSO characteristics are not seen in traumatic onycholysis or nail psoriasis: proximal margin of the onycholytic area with jagged edge and sharp structures directed to the proximal fold; longitudinal striae of different colors in the onycholytic nail plate; and overall appearance of the color of the affected nail plate in a matted variable discoloration resembling the aurora borealis.

CLSM (confocal laser-scanning microscopy) is a new diagnostic technique. The CLSM aspect of dermatophytes appears as a network of long structures with high reflection and the typical shape of hyphae: the CLSM aspect of yeasts has been reported by Arrese et al., whereas moulds have not yet been described in nails.

Other novel diagnostic tools for onychomycosis include the dermatophyte test strip, fluorescence microscopy, and Raman spectroscopy. The dermatophyte test strip is an immunochromatography test that employs a monoclonal antibody that reacts with Trichophyton species and provides a positive signal after 15 minutes of contact with one of these dermatophytes. It is a ready-to-use kit that is quick, simple, and inexpensive. Because the test has a high sensitivity and a negative predictive value, it can be used to rule out onychomycosis in all suspicious cases.

The method had previously been tested in a small series on onychomycosis.

Treatment

Onychomycosis treatment is determined by the clinical type, the number of involved nails, and the severity of the infection. The disadvantages of therapies include the fact that oral treatments are frequently limited by drug interactions and potential hepatotoxicity, and topical antifungals have limited efficacy when used without nail plate debridement. A combination of oral and systemic treatment is frequently the best option.

Topical Treatment

A transungual delivery vehicle is required for the penetration of a topical antifungal through the nail plate. The inability of topical antifungal agents to penetrate the nail unit limits their use, and relapses and re-infections are common, occurring in at least 20%-25% of patients.

In severe onychomycosis, combining systemic antifungals, debridement, or nail avulsion reduces treatment duration and increases cure rate. Nail lacquers are effective in the treatment of WSO and DLSO limited to less than 50% of the distal nail in monotherapy. The treatment period lasts 6 to 12 months. Amorolfine 5% or ciclopirox 8% in non-water-soluble lacquers and ciclopirox in water-soluble nail lacquer are two options. Amorolfine nail lacquer is used once a week, whereas ciclopirox nail lacquer is used every day. Fungistatic and fungicidal properties of amorolfine against dermatophytes, non-dermatophytes, moulds, and yeast. Gupta et al. recommend amorolfine 5% nail lacquer for onychomycosis without matrix involvement and mild cases of distal and lateral subungual onychomycosis affecting up to two nails.

Ciclopirox has antifungal, anti-inflammatory, and anti-allergic properties. It is used every day. There are two formulations that improve nail permeability: ciclopirox 8% in non-water-soluble lacquers and ciclopirox in water-soluble nail lacquer.

New topical antifungals for the treatment of dermatophyte-induced onychomycosis include efinaconazole 10% solution and tavaborole 5% solution. Efinaconazole 10% nail solution is a promising drug for toenail onychomycosis that was approved by the FDA in June 2014. It is a new triazole antifungal that is applied topically once daily without nail debridement to treat mild to moderate DLSO. Cure rates are comparable to those seen with itraconazole taken orally. A recent study looked at the efficacy of this nail lacquer on 1655 patients with onychomycosis for 52 weeks and discovered that efinaconazole was more effective at treating the disease in its early stages.

Systemic Treatment

Systemic treatment is required for DLSO that extends to the proximal nail, PSO caused by dermatophytes, and deeply infiltrating white superficial onychomycosis. Fluconazole, itraconazole, and terbinafine have improved treatment success, resulting in a mycological cure in more than 90% of fingernail infections and approximately 80% of toenail infections. The clinical characteristics of the onychomycosis (total onychomycosis, very thick subungual hyperkeratosis, and dermatophytoma, which make it difficult for the drug to reach the affected area in active concentration), etiological agents (several non-dermatophytes, including Neoscytalidium, Scopulariopsis, and Fusarium sp., do not respond to systemic antifungals), and (immunodepressed patients have a poor prognosis, and several drugs may modify antifungal blood levels).

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Terbinafine can be given as a continuous therapy of 250 mg per day for 12 weeks or as a pulse therapy of 500 mg per day for four weeks on and four weeks off. Itraconazole is given in pulse therapy at a dose of 400 mg daily for one week every month. The treatment period for fingernails is two months and three months for toenails.

Continuous terbinafine and itraconazole pulse therapy are both effective and safe treatments for dermatophyte toenail onychomycosis in diabetics. These regimens are compatible with topical nail lacquers. There have been no studies that compare the cure rates of systemic and topical antifungals in combination, but these combinations are commonly used in clinical practise. Periodic removal of the affected nail plate by a podiatrist or topical application of urea ointment can hasten healing. Recurrences and reinfections are common (affecting up to 20% of cured patients).

Fluconazole is also used to treat dermatophyte onychomycosis at a dose of 150-300 mg weekly for more than six months, but it is less effective. Fluconazole, itraconazole, and terbinafine have a favourable safety profile. Posaconazole and albaconazole are new drugs that could be used as an alternative therapy.

Non-dermatophyte moulds do not respond to systemic antifungals in general, so topical therapy combined with periodic removal of the affected nail plate is the best option in these cases of onychomycosis. Terbinafine should not be used to treat onychomycosis caused by Candida sp. because the yeast is not sensitive to it. Furthermore, the isolation of Candida from a nail should always be accompanied by a thorough examination of the patient, as Candida onychomycosis is frequently associated with diabetes or immunodeficiency.

Onychomycosis treatment takes several months because the nail grows slowly, especially in the elderly. The type and severity of onychomycosis, as well as the patient's comorbidities, influence drug selection. The majority of patients present with a DLSO caused by dermatophytes involving the distal part of one or two great toe nails, and the treatment of choice is topical antifungal application, possibly in conjunction with periodic removal of the affected nail plate.

CONCLUSIONS

Onychomycosis is a common fungal infection that requires specialised treatment. Therapy takes several months because the nail grows very slowly, particularly in the elderly. The type and severity of onychomycosis, as well as the patient's comorbidities, influence drug selection. The majority of patients present with a DLSO caused by dermatophytes involving the distal part of one or two great toe nails, and the treatment of choice is topical antifungal application, possibly in conjunction with periodic removal of the affected nail plate. We recommend systemic treatment with fluconazole, itraconazole, or terbinafine for DLSO that extends to the proximal nail, PSO caused by dermatophytes, and deeply infiltrating white superficial onychomycosis.

More research on lasers and photodynamic therapy is required before their use can be standardised.

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