Chapter 3
Distal Subungual Onychomycosis

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Key Features
- More than 85 % of all fungal nail infections (onychomycosis) present as distal lateral subungual onychomycosis (DLSO).
- Major predisposing factors are age, diabetes, and peripheral vascular disease.
- The general clinical presentation of DLSO is discoloration of the nail, subungual hyperkeratosis, and onycholysis.
- DLSO is easy to confuse with other nail dystrophies that mimic its appearance (i.e., trauma, psoriasis, lichen planus, etc.). Therefore, KOH, fungal culture, or PAS stain is necessary to confirm the diagnosis.
- Recurrence and reinfection are common.

Introduction

Distal lateral subungual onychomycosis (DLSO) is the single most common form of fungal nail infection and accounts for approximately 41 % of *all* nail abnormalities [1]. It is classically characterized by fungal invasion of the nail bed from under the free edge of the nail (the hyponychium), often as an extension of tinea pedis (Fig. 3.1). This causes subungual hyperkeratosis, thickening and discoloration of the nail plate, and eventual onycholysis (detachment of the nail from the nail bed).

Although not life threatening, these ugly, unsightly nails are evidence of a deceptively complex condition that can cause considerable pain and make it difficult to

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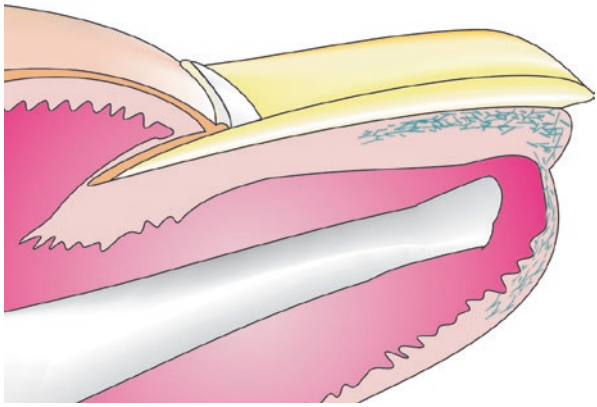

Fig. 3.1 This schematic illustrates the progression of fungal infection in DLSO, specifically how the fungus gains access to the nail bed via the hyponychium

perform simple daily activities like walking and wearing shoes. Additionally, if allowed to progress, DLSO can cause significant complications, including bacterial superinfection and cellulitis.

Aside from the physical symptoms, it's also important to keep in mind the powerful psychosocial impact DLSO can have on quality of life. Many patients report feelings of severe embarrassment over the appearance of their fungal nails, problems with self-esteem, and social withdrawal [4, 5]. Recent surveys confirm that people who suffer from onychomycosis are more likely to be excluded from social activities, and are perceived by others as less likely to be able to form good relationships as well as less likely to succeed at work [6].

Sadly, despite the potential complications and obviously diseased appearance of infected nails, DLSO is often dismissed as "merely" a cosmetic problem and is commonly ignored or incompletely treated. This may have something to do with the fact that fungal infections of the nail are notoriously difficult to cure, partially due to factors inherent to the nail itself: the sluggish growth of the nail means diseased portions are slow to be replaced, and the hard, protective nail plate inhibits topical drugs from reaching the fungal pathogens on the nail bed beneath it. Also, patients are regularly plagued with recurrences and reinfections [2, 7], and, faced with a choice between oral systemic medications requiring laboratory monitoring for toxicity, or lengthy topical therapies that often require nail debridement and multiple return visits, many patients are – unsurprisingly – noncompliant. This further complicates the course of the disease.

Although DLSO can occur in either the fingernails, toenails, or both, toenails are overwhelmingly more often affected, with a toenail to fingernail ratio of 19:1 [1]. The vast majority of toenail fungal infections (greater than 90 % of cases) are caused by dermatophytes (parasitic fungal organisms that feed on keratin), but they can less frequently be caused by non-dermatophytic molds and yeasts. The causal organisms of fingernail onychomycosis are almost exclusively dermatophytes.

Epidemiology

Unfortunately, it's difficult to quantify the exact prevalence of DLSO, as estimates vary widely from study to study (ranging from 2 to 13 %) [1, 8–15]. This is partly because DLSO (and onychomycosis in general) is highly dependent on geographic location, and partly due to differences in study methodology, like the population source (e.g., were they patients who presented with nail complaints, or simply those in for regular checkups?). As a matter of fact, some have even suggested that – while it is undeniably common – the general prevalence of fungal nail infections has been slightly overestimated by hospital-based studies [10].

That being said, there has *clearly* been a steady upward trend in the past few decades. In 1979, a population study in North America reported the prevalence of onychomycosis to be just over 2 % [16]. Less than 20 years later, that number had jumped to more than 8.5 % [8]. More recently, a large multicenter study reported it to be 13.8 % [9]. Considering that DLSO accounts for greater than 85 % of all onychomycosis cases, this directly translates into a rising incidence of DLSO. This burgeoning growth can be tied to changes in the culture of modern society, first among them an increase in our use of occlusive footwear which provides a warm, moist, confined environment that is highly conducive to fungal growth. Onychomycosis prevalence (and, by extension, DLSO) has actually been shown to decrease in populations wearing nonocclusive footwear, like sandals [17]. Another factor in the spread of fungal infections like DLSO is the increasing popularity of public pools, fitness center locker rooms, etc., where wet floors provide favorable breeding grounds for fungi and people are often barefoot [18].

Multiple studies have noted that family members of patients infected with DLSO have a higher risk of contracting the disease [19]. Initially, it was believed that this higher risk was *solely* due to intrafamilial transmission, i.e., increased exposure to a reservoir of infection. However, more recent studies have indicated that DLSO has a genetic component: susceptibility to infection by *Trichophyton rubrum* appears to be inherited in an autosomal dominant pattern [20, 21]. Subsequent studies identified specific genotypes affecting the immune system that prevent "the production of a full adaptive immune response," leaving these individuals susceptible to fungal overgrowth and chronic infections [22].

Additionally, several studies have observed that men are almost three times more likely to develop onychomycosis than women [23]. Although the reasons for this gender difference aren't fully understood, it likely involves social and/or genetic factors.

Aside from culture, environment, and genetics, the greatest predisposing risk factor for DLSO appears to be advanced age, as several studies have shown an increased prevalence of onychomycosis with increasing age [1, 3]. The rate of fungal nail infections in the general population is approximately 10 %, but in adults over age 70, that number can climb as high as 50 % [2, 3]. This is most likely explained by the fact that the nail grows slower with aging and infection can progress easily. Common comorbidities seen in the elderly are also risk factors for

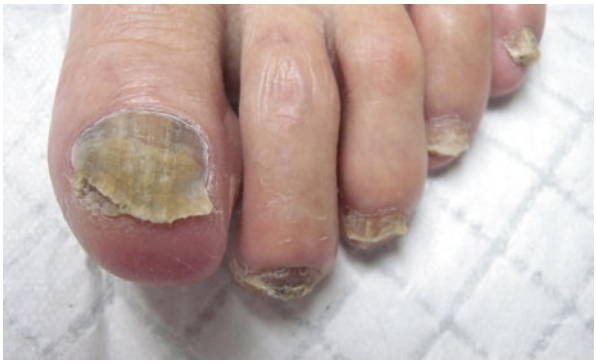

Fig. 3.2 DLSO in a diabetic patient. All nails are affected. Note the tinea pedis scaling and the hematoma of the great toe (due to poor fitting shoes, which is common due to neuropathy)

DLSO, including poor peripheral circulation, diabetes, decreased immune function, repeated nail trauma, longer exposure to pathogenic fungi, and even the simple inability to maintain good foot care.

It's therefore unsurprising that children are rarely affected by DLSO. A prospective, multicenter survey found the prevalence of fungal nail infections in North American children 18 years old or younger to be less than .5 % [24]. Aside from the fact that there is a relative absence of the previously listed common DLSO risk factors in young people, reasons for the incredibly low infection rate compared to adults can also be explained by their lower prevalence of tinea pedis, faster nail growth, and generally smaller nails, which provide less surface area for fungal invasion.

As mentioned, diabetes is a notable underlying comorbidity in patients with DLSO. Approximately one-third of diabetics have a fungal nail infection, and they are 2.77 times more likely to develop onychomycosis than their nondiabetic counterparts (Fig. 3.2) [23]. Also, their impaired wound healing and sensory neuropathy put them at higher risk for more serious, limb-threatening complications. The jagged edges of their thickened, brittle nails can injure the surrounding soft tissue and create an unnoticed entry point for bacteria, fungi, or other pathogens, resulting in significant infections that may eventually lead to the need for amputation [25]. Retrospective studies have determined that diabetics with fungal infections like DLSO are approximately 3–5 times more likely to develop foot ulcers and/or gangrene than diabetics without onychomycosis [26].

It's particularly important to keep in mind the relationship between DLSO and tinea pedis [7]. The same dermatophyte organism (*Trichophyton rubrum*) is the major cause of both fungal infections [10, 27], and therefore each condition can serve as a reservoir of infection for the other. That's why DLSO is almost always preceded (or accompanied) by an infection of tinea pedis (Fig. 3.3). This relationship partially explains the greatly increased frequency of toenail compared to fingernail DLSO: the greater incidence of tinea pedis over tinea manuum provides more opportunities for the toenails to be infected.

Of course, if patients scratch or pick at their fungally infected feet, toes, or toenails, it's possible for them to transfer the fungus onto their hands, which can cause

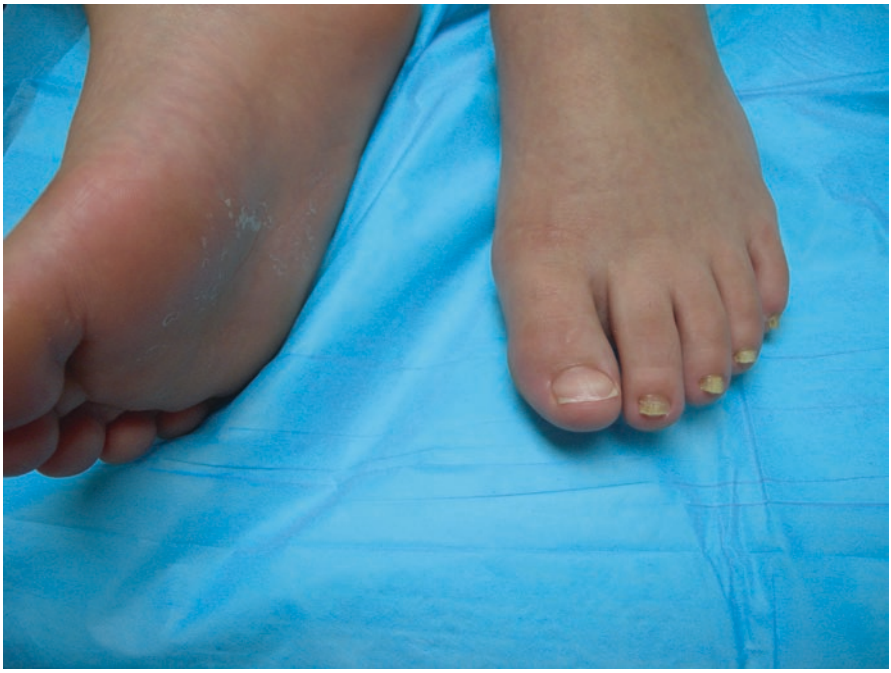

Fig. 3.3 DLSO and concomitant tinea pedis on the plantar surface of the opposite foot due to *T. rubrum*

Fig. 3.4 An example of fingernail DLSO

them to develop tinea manuum and/or fingernail DLSO (Fig. 3.4). This often causes the patient to develop a relatively common pattern of infection known as "two feet-one hand syndrome (Fig. 3.5)" [28, 29].

Overall, the incidence of DLSO is projected to continue increasing, largely due to a surge in critical risk factors like the age of the population, along with an increased prevalence of diabetes and peripheral vascular disease.

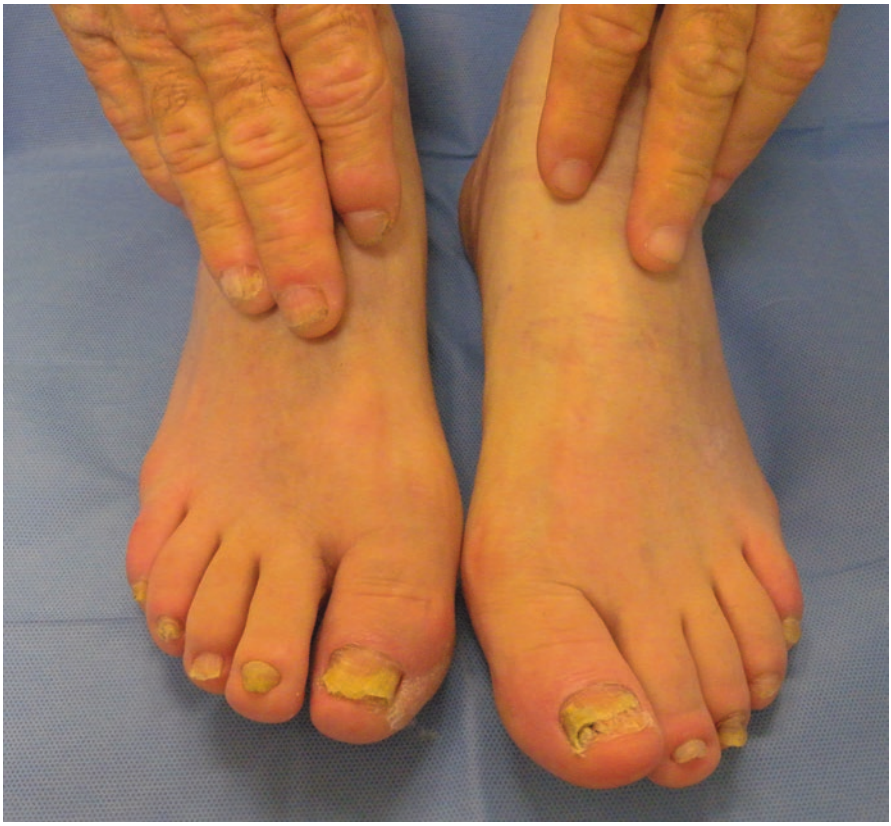

Fig. 3.5 DLSO is present on the nails of both feet and the right hand, while the left hand is unaffected (two feet-one hand syndrome)

Clinical Features

The characteristic features of DLSO are discoloration of the nail, subungual hyperkeratosis, and onycholysis (Fig. 3.6).

True to its name, DLSO's fungal organism invades the nail bed at the distal portion of the nail. The fungus usually first infects the palm or sole, causing tinea pedis or tinea manuum, and then spreads from the skin to the nail bed via the hyponychium or the lateral nail fold.

In the early stages of infection, the fungus is limited to the nail bed, and the nail plate may appear normal. During this time, the stratum corneum of the nail bed often begins to thicken (subungual hyperkeratosis) due to mild inflammation from the fungal infection. The resulting keratotic debris pushes the nail plate up, eventually causing onycholysis.

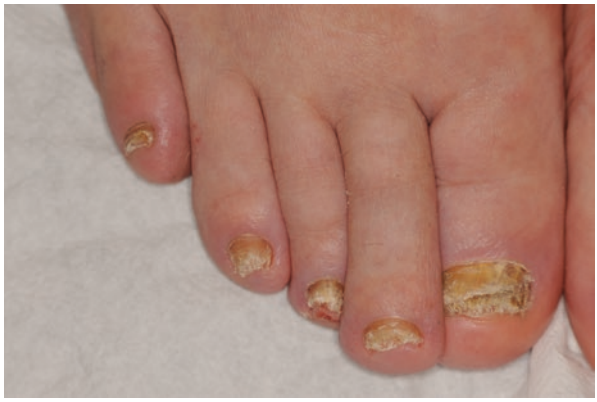

Fig. 3.6 DSLO. Note the yellow discoloration, severe subungual hyperkeratosis, and onycholysis

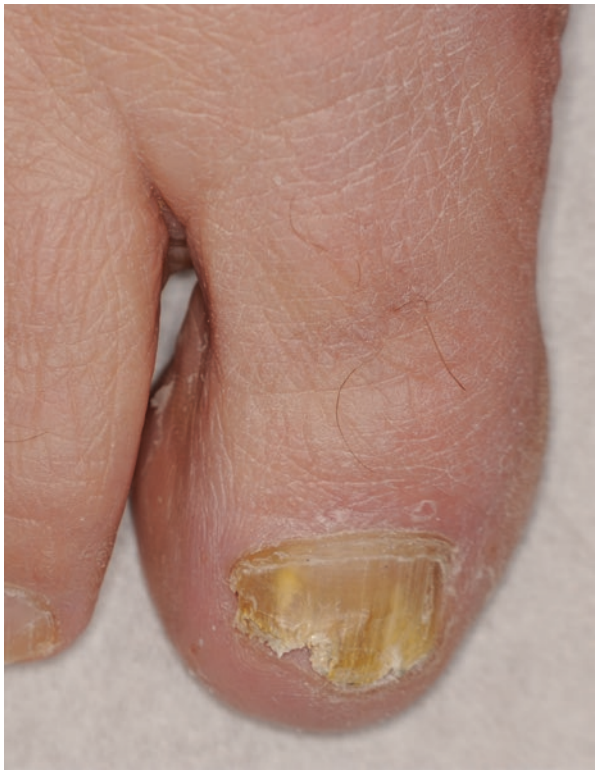

Fig. 3.7 The proximal progression of the fungus causes the yellow streaks leading toward the proximal nail fold. Also, note the tinea pedis scaling

From the initial site of infection, fungi migrate proximally (toward the cuticle) along the longitudinally oriented rete ridges of the nail bed. This explains the yellow, orange, or white longitudinal spikes and streaks which are a typical sign of progressing disease (Figs. 3.7 and 3.8).

The nail plate may also display diffuse discoloration and look yellow, orange, or white. Less commonly, when DLSO is caused by non-dermatophytic fungal molds that produce melanin, the nail presents with a brown/black pigmentation (ungual

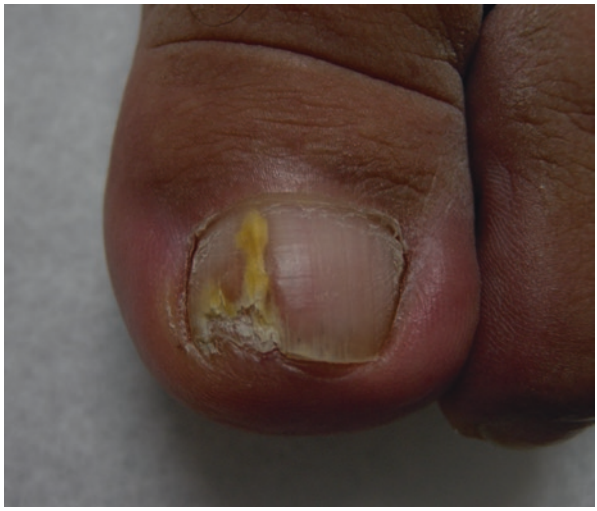

Fig. 3.8 Another example of a discolored longitudinal streak due to proximal fungal progression, this one extending all the way into the lunula. There is also subungual hyperkeratosis

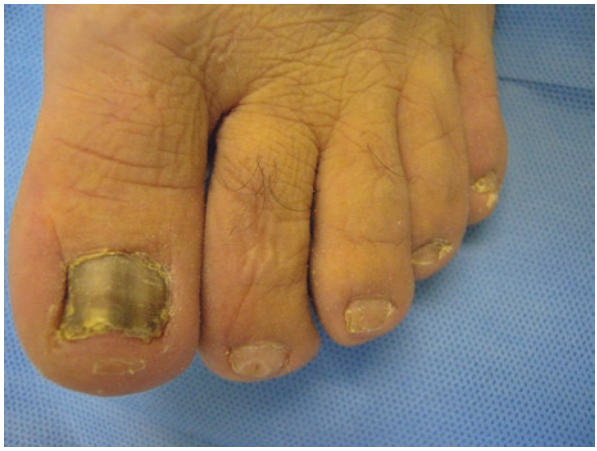

Fig. 3.9 Pigmented DLSO

melanonychia) similar in appearance to nail melanoma (Fig. 3.9). Thankfully, this is relatively rare, as many of the organisms which cause ungual melanonychia (e.g., *Neoscytalidium dimidiatum*) do not respond to antifungal therapies and are very difficult to cure [30].

Sometimes dermatophytomas (rounded or linear areas of particularly dense discoloration) are observed (Figs. 3.10 and 3.11a,b). This is generally a more advanced form of the disease and is considered a negative prognostic factor. A dermatophytoma indicates a fungal abscess (a mass of hyphae and spores) under the nail. The fungi in these masses create a biofilm and are particularly difficult to treat without debridement.

In time DLSO can progress to total dystrophic onychomycosis (TDO) characterized by a thickened and crumbled dystrophic nail. However, as patients often cut the detached nail plate, particularly in fingernails, clinical presentation can be less typical (Fig. 3.12).

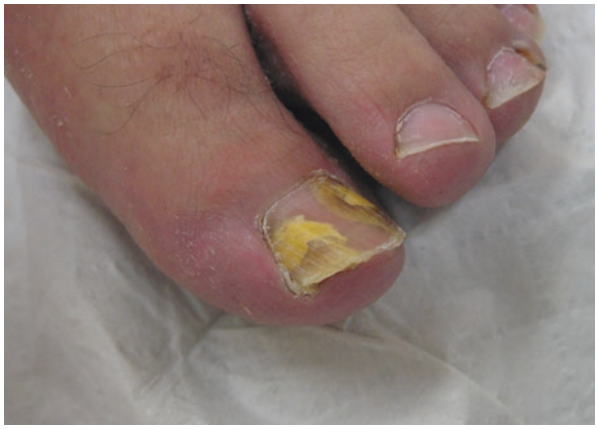

Fig. 3.10 Note the prominent dermatophytomas on the great toe

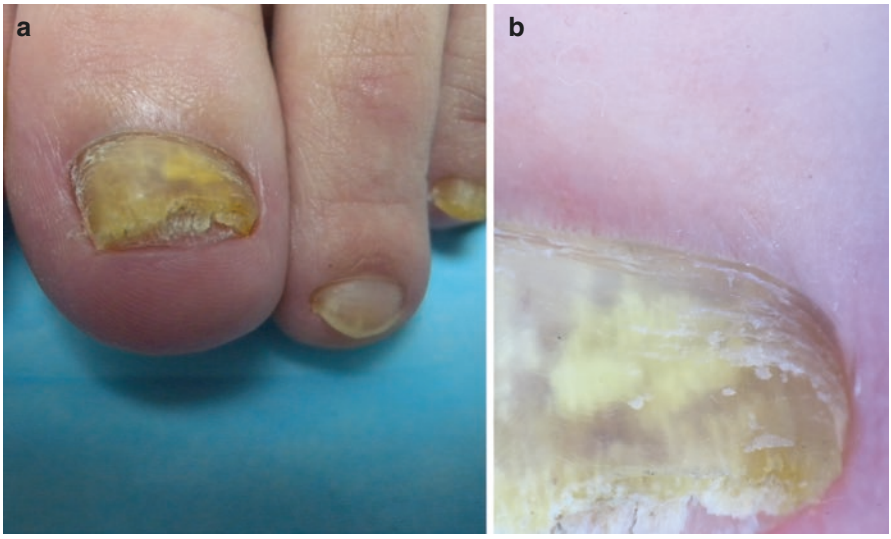

Fig. 3.11 (**a**, **b**) Nail discoloration, subungual hyperkeratosis, onycholysis, and a dermatophytoma (**a**). A dermatoscopic image of a patch that doesn't reach the free margin of the nail (**b**)

Several specific clinical findings are considered factors that predict a poor response to treatment. These include dermatophytomas, cases where greater than 50 % of the nail is affected (especially if there is significant involvement of the lateral nail), cases with more than 2 mm of subungual hyperkeratosis, as well as those cases where the disease has progressed to TDO with matrix involvement. Other negative prognostic factors have to do with the fungal organism itself (e.g., a *Neoscytalidium* mold, as discussed above) or are patient specific – those with immunosuppression or diminished peripheral circulation have a higher likelihood of treatment failure.

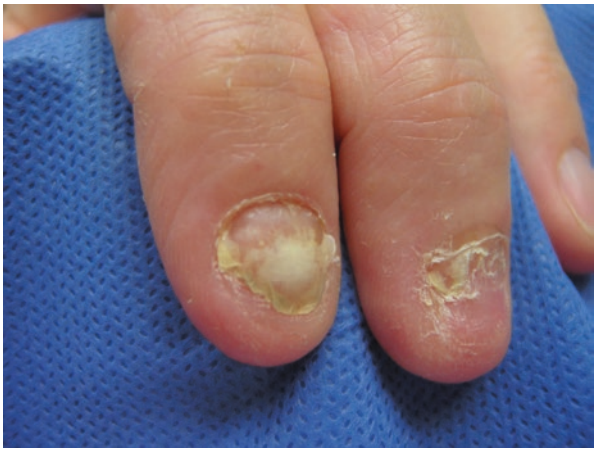

Fig. 3.12 Fingernail DLSO where the patient cut the affected nail

The severity of infection can also be determined using the onychomycosis severity index (OSI). This simple scoring system takes into account the percentage of affected onychomycotic nail, the proximity of infection to the nail matrix, and the presence of either dermatophytomas, longitudinal streaks, or greater than 2 mm of subungual hyperkeratosis, and calculates a score from 1 to 35. Mild disease is classified by a score of 5 or below, moderate disease by 6–15, and severe disease by 6–35 [31]. By providing an objective measurement of disease severity that can be quickly assessed as the clinical picture changes, patients can be followed more accurately throughout their course of treatment.

Diagnostic Clues

Making a conclusive clinical diagnosis of DLSO can be difficult, as many of its classic features (nail discoloration, subungual hyperkeratosis, onycholysis, and thick, damaged, brittle nails) are also seen in other nail dystrophies (e.g., trauma, psoriasis, lichen planus, onychogryphosis, etc.). However, the mechanisms of fungal progression provide plenty of clinical signs that can suggest a diagnosis of DLSO and indicate the need for further confirmatory laboratory testing.

As the fungus usually first infects the palm or sole and only then spreads to the nail bed, first inspect the skin on the soles, fingertips, and between the toes for signs of tinea pedis/tinea manuum scaling. While the absence of scaling doesn't necessarily rule out a diagnosis of DLSO, its presence can help in making a positive diagnosis.

Once the fungus invades the nail bed and the stratum corneum begins to thicken, subungual hyperkeratosis causes onycholysis. The keratotic debris lifting the nail creates a unique appearance under the free edge of the nail that De Crignis et al. call "ruin appearance" [32]. By inspecting the hyponychium with a dermatoscope, this

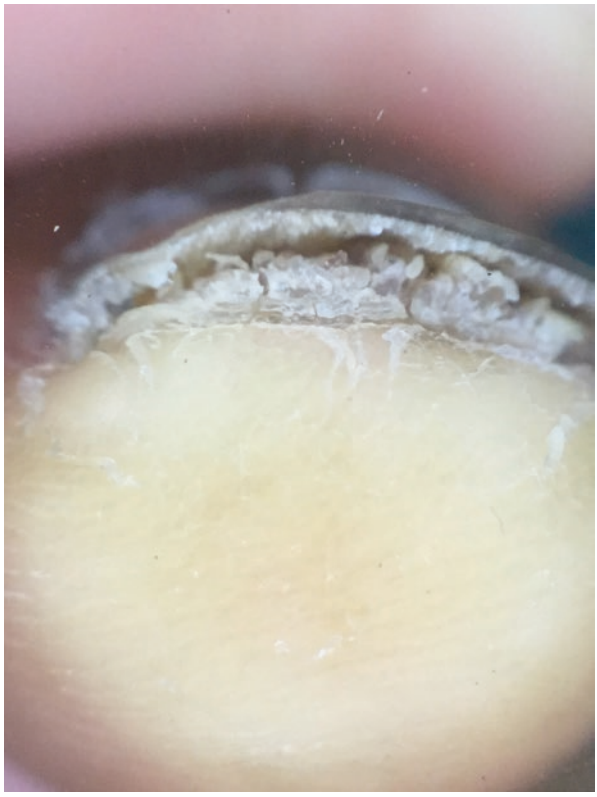

Fig. 3.13 A dermatoscopic image of the distal border of the nail showing "ruin appearance"

appearance can be clearly visualized (Fig. 3.13). Again, the absence of ruin appearance doesn't necessarily rule out a diagnosis of DLSO; however, its presence is *very* indicative of a positive diagnosis.

As the fungus advances longitudinally along the rete ridges of the nail bed, it causes a specific longitudinal pattern of discoloration which provides an easy, non-invasive method to differentiate between DLSO and conditions which merely mimic the appearance of DLSO, e.g., traumatic onycholysis, the second most common nail dystrophy. When examining the nail, use a dermatoscope to inspect the most proximal edge of the discolored/onycholytic area for an uneven border with sharp projections towards the proximal nail fold (Fig. 3.14). This visual cue (dubbed by Piraccini et al. as a "jagged edge with spikes") is distinct and exclusive to DLSO thanks to the behavior of the migrating fungus. Traumatic onycholysis presents with a smooth, linear edge without indentations [33, 34].

Another dermatoscopic finding caused by the proximally migrating fungus is an irregular matte pigmentation distributed in longitudinal striae on the detached nail plate. Since it forms a pattern similar to an aurora borealis, it was labeled by Piraccini et al. as an "Aurora Pattern." Its presence is also highly suggestive of DLSO [33].

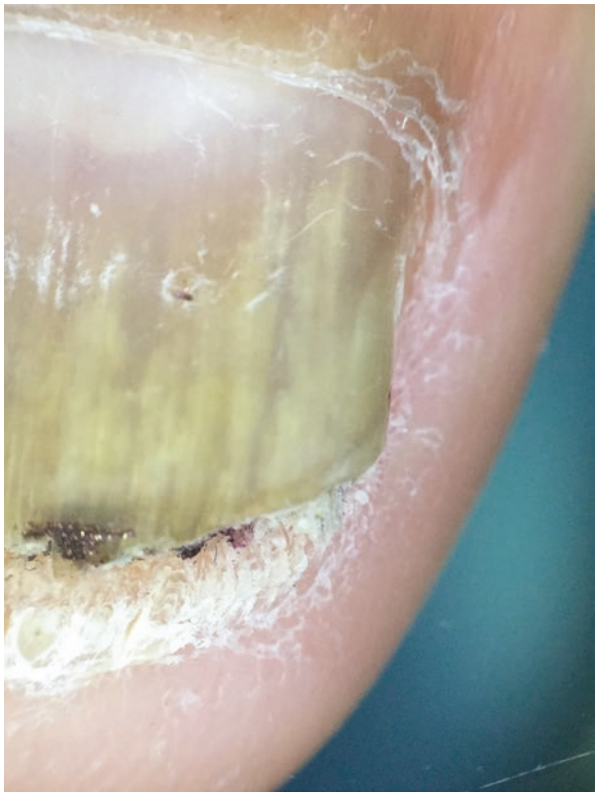

Fig. 3.14 A dermatoscopic image exhibiting "spikes" on the proximal margin, imbuing it with the "jagged edge" appearance

Summary for the Clinician

DLSO is incredibly common and can cause significant physical and psychosocial problems. Due to increasing incidence of important risk factors, we expect to see a concomitant increase in DLSO cases in the years to come.

Since only about half of all nail abnormalities can be attributed to fungal infections, it's important to be able to distinguish between true DLSO and other conditions that merely mimic its appearance before beginning treatment – which can be long, difficult, and expensive.

Unfortunately, the close similarities between many of the nail dystrophies tend to make obtaining a definitive clinical diagnosis very challenging. Therefore, while the clinical presentation combined with dermoscopy and a suggestive history can strongly point you in the direction of DLSO, the diagnosis needs to be confirmed by laboratory techniques [35].

Today, that means KOH, fungal culture, or a PAS stain. In the future, however, newer PCR techniques will probably be utilized more often, as they have advantages over all of those methods: PCR is faster (results are returned in days vs. weeks), unaffected by fungal viability, and is less susceptible to contamination.

Another reliable method is the dermatophyte test strip, shown to have an overall concordance rate of 95 % [36]. Keep in mind that these test strips will only identify dermatophyte infections, but those do account for the vast majority of onychomycosis cases.

Clinical Pearls

- If you see tinea pedis, look for onychomycosis.
- If someone comes in with fingernail disease, look at his or her toenails, and vice versa.
- Tell affected patients to put on their socks before their underwear to prevent transfer of fungus to the inguinal folds, causing tinea cruris.
- Although women and children have a lower incidence of infection, they are more likely to seek treatment. Ask them about other members of their family, as it's likely some will be infected.

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