Nail disease

Is it fungal? If so, what should I do?

There are many causes of nail dystrophy, and a careful evaluation will assist in reaching the correct diagnosis and assessing the need to treat. Not all nail disease is caused by a fungal infection, but physicians need to know what to do when it is.

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Nail dystrophy is very common in the adult population and is also seen in children. A fungal infection is the most common cause in toenails; however, this is not the case for fingernails, which have many causes of dystrophy including frequent hand wetting, psoriasis and other cutaneous conditions.

Understanding the structure of the nail unit is helpful in visualising the location of pathology. A guide is shown in the box on page 43.

Presentation

The most common presentation is a patient who finds his or her fingernails or toenails to be cosmetically unacceptable. Concern about the appearance of the nails occurs in both men and women, and in all age groups except small children. Often these patients have heard from friends that the problem is easy to solve or have seen advertising that suggests so. Many have already had nail clippings taken for fungal culture and potassium hydroxide (KOH) microscopy, with negative results.

Diagnosis

The first steps in evaluation involve taking a careful general medical history and examining the skin fully.

If only one nail is involved, the differential diagnosis includes benign and malignant tumours that can, depending on their position, alter the nail growth. Distal lifting of the nail (onycholysis) can be caused by any growth at the hyponychium – the most common is a subungual wart. A tumour of the nail bed will discolour the nail and may induce pain – examples include a glomus tumour or an exostosis (Figure 1). If the nail plate is being destroyed then intraepithelial squamous cell carcinoma (Bowen's disease) and amelanotic melanoma, although rare, need to be remembered (Figures 2a and b); an adequate biopsy will be required.

Single nail lifting with no underlying tumour may be due to psoriasis (Figure 3). Primary irritant dermatitis due to frequent hand wetting (either occupational or at home) may begin with

IN SUMMARY

- **If a single nail plate is destroyed, consider Bowen's disease and malignant melanoma.**
- **Nail dystrophy may be caused by psoriasis. Ask the patient about a family history and look for the presence of other signs.**
- **Oral therapy to clear the toenails of fungal infection is important in patients who have diabetes, are immunosuppressed or have a history of recurrent cellulitis.**
- **If there is recurrent tinea at other sites, check the toenails – these may be the source of the recurrences. If the fingernails on only one hand are involved, check the toenails (usually both feet are involved).**
- **The side effect profile of the medication must be weighed against the desire to treat a purely cosmetic problem.**

one nail of the dominant hand showing onycholysis, and other evidence of hand dermatitis may be present. The use of artificial nails can lead to onycholysis (Figure 4); trauma to the cuticle (proximal nail fold) by habitual picking or accident will also result in a specific nail defect (Figure 5).

When multiple nails are involved, it is important to examine the entire skin, including the scalp, oral mucosa, inguinal folds and natal cleft. Evidence of psoriasis in the scalp or fold areas is helpful; nail pitting also points to this diagnosis (Figures 6a and b). Maceration between the toes is typical of a dermatophyte infection (Figure 7); annular lesions of the inguinal folds, buttocks or legs are suggestive of a fungal infection.

It is important to check the toenails if a large area of tinea is present elsewhere (Figures 8 and 9) or if the fingernails of one hand only are involved – in these situations the toenails are frequently involved and are the source of the infection (Figure 10). Involvement of the nails or skin of one hand only is suggestive of a fungal infection. Lichen planus can affect the nails (Figure 11a); a white lacy pattern on the buccal mucosa may be suggestive (Figure 11b). A hand dermatitis and paronychia suggest that hand wetting and atopic dermatitis may be contributing problems.

Anatomy of the nail unit

The structure of the nail unit is shown in Figure A. The nail is a transparent plate composed of keratin that is produced by cell division in the nail matrix. The matrix, which lies deep to the proximal nail fold, is partly visible as the lunula. The plate is firmly adhered to the nail bed, which is not thought to contribute significantly to the formation of the nail. The cuticle forms a seal between the nail plate and proximal nail fold, preventing the penetration of extraneous material. The nail plate ends and loses its bond to the nail bed at the hyponychium.

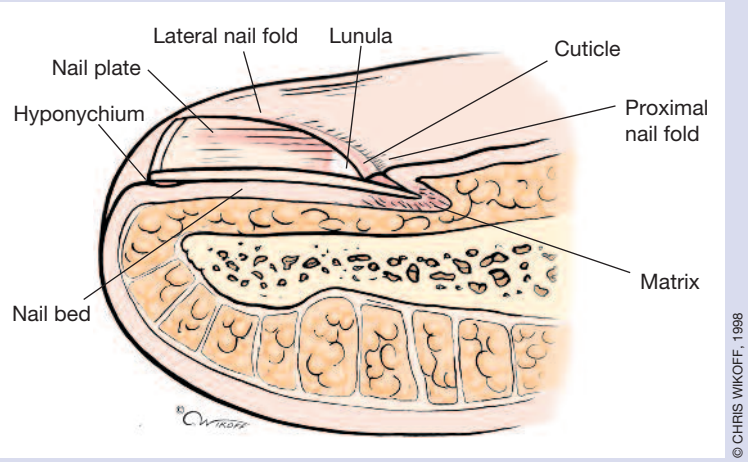

Figure A. Sagittal section through a normal nail.

Investigations

If a fungal infection is suspected in nail disease, scrapings and clippings should be taken for KOH microscopy and culture. In addition, skin scrapings should be taken if other evidence of tinea is present, such as maceration between the toes, erythema and scale of the soles (sometimes associated with pustules and often with asymmetrical annular lesions on the legs) or an asymmetrical annular eruption extending from the inguinal fold.

Before taking scrapings or clippings, ask whether any topical antifungal agent has been applied within the last week. Such preparations are readily available over the counter and will contribute to a false negative result on microscopy and culture. The percentage of specimens that yield false negative results is far greater for nail clippings than for skin scrapings.

The skin scrapings are best collected using a number 10 scalpel blade. Nail clippings are best obtained as close to the normal remaining nail as possible – this is the growing edge and hence the fungus is more likely to be viable. The scrapings or clippings should be collected over a black cardboard surface and then placed in a package and sealed. The specimens survive well and are easily transported, so this procedure is applicable in isolated rural areas.

Management

When the infection is very superficial and can be almost completely scraped off with a blade, a topical antifungal lacquer such as amorolfine (Loceryl Nail Lacquer) may be helpful. A varnish will provide better penetration than a tincture. However, if the nail is very thickened with subungual hyperkeratosis and severe dystrophy, one of the newer oral antifungal agents will be required to treat the fungal component.

Oral treatment may be the only effective treatment for more severely infected toenails. A systematic review published in 2000 found little evidence of effectiveness of topical therapies for fungal toenail infections.[1]

Figure 1. Subungual exostosis.

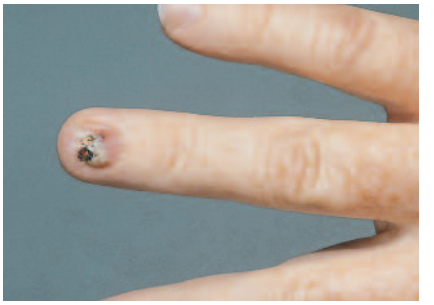

Figure 2a. Subungual malignant melanoma.

Figure 2b. Acral lentiginous melanoma.

Figure 3. Psoriasis of the nails.

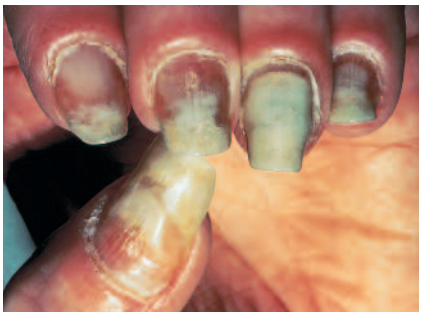

Figure 4. Onycholysis from sculptured nails.

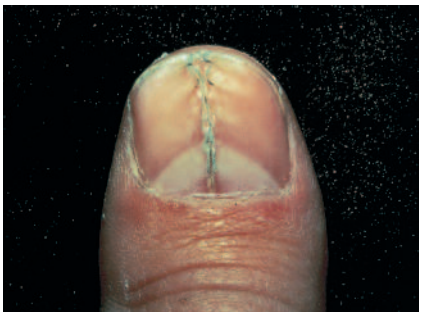

Figure 5. Nail defect caused by a habit tic.

Griseofulvin

For many years, griseofulvin (Griseostatin, Grisovin) was the only oral therapy available for treating onychomycosis. Griseofulvin is inexpensive and useful for many cutaneous dermatophyte infections, but its action is fungistatic only and so the administration time is protracted. Griseofulvin has largely been superseded by newer drugs – the azoles and allylamines – for nail disease.

Terbinafine and itraconazole

Last year, a systematic review was published of 32 randomised trials of oral treatments for fungal infections of the toenails.[2] The reviewers found that terbinafine (250 mg/day) was more effective than itraconazole (400 mg/day), as assessed by mycological cure rates at 12 months after a three-month course of treatment. They found no evidence that intermittent regimens of itraconazole produced statistically significant equivalent cure rates compared with continuous schedules, nor any evidence that intermittent regimens or shorter treatment times resulted in fewer reported adverse events. The reviewers concluded that a continuous regimen of terbinafine (250 mg/day) is the most effective oral therapy for long term management of fungally infected toenails.

Based on the conclusions of the review,

Figure 6a. Psoriasis affecting multiple nails.

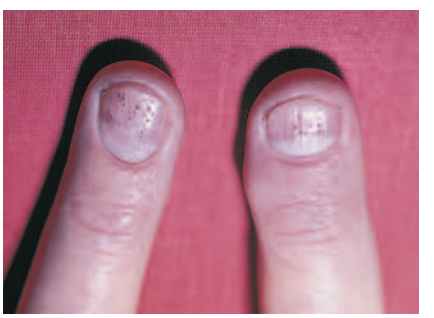

Figure 6b. Nail pitting in psoriasis.

Figure 7. Fungal infection of the small toenail associated with plantar and interdigital involvement.

Figure 8. Facial fungal infection – remember to examine the toenails.

Figure 9. Toenails of a patient with skin tinea.

Figure 10. One handed fungal infection of nails.

the initial treatment of choice for a confirmed fungal infection of the toenail would be terbinafine hydrochloride (Lamisil Tablets) – that is, if a decision is made to treat. This is probably more effective for fingernail dermatophyte infections because fingernails grow faster than toenails and poor circulation is more of an issue with the latter. Terbinafine, a synthetic antimycotic agent belonging to the allylamine family, is a broadspectrum agent that is primarily fungicidal and highly active against dermatophytes.

Terbinafine is highly lipophilic and keratophilic and is well absorbed from the gut. The treatment is generally well tolerated, with mild and transient gastrointestinal symptoms being reported. However, severe skin reactions have been described, including pustular reactions, Stevens–Johnson syndrome and toxic epidermal necrolysis, and there are also reports of headache, loss of taste, severe neutropenia and hepatic injury. The US FDA recommends that liver function tests be performed prior to and six weeks after starting oral terbinafine.

If a patient has a history of one of these side effects and he or she still wishes to treat the fungal nail infection, the next

Figure 11a. Lichen planus destroying the nail.

FIGURE 11a REPRINTED WITH PERMISSION FROM THE AMERICAN ACADEMY OF DERMATOLOGY, ALL RIGHTS RESERVED. FIGURE 11b COURTESY OF PROFESSOR STEVEN KOSSARD, SYDNEY.

Figure 11b. Lichen planus. White lace-like pattern and erosive patches on the buccal mucosa and lips.

option would be oral itraconazole (Sporanox Capsules), a triazole antifungal agent. The side effects of itraconazole include gastrointestinal symptoms, leucopenia, hypertension, hepatic injury and pustular skin reactions. Itraconazole significantly elevates the plasma levels of digoxin, cyclosporin, felodipine and midazolam. Coadministration of itraconazole with lovastatin, simvastatin, astemizole, cisapride, midazolam, triazolam or terfenadine, for example, is contraindicated.

Assessing the need to treat

If the result of KOH microscopy or culture is positive for a dermatophyte then the option to treat exists. Patients need to be fully informed of potential side effects and drug interactions to help them decide whether to treat a proven fungal infection with oral antifungal agents, especially if the problem is cosmetic only. In particular, if there is any evidence of psoriasis, it is important to explain that the oral antifungal agent will treat only the fungal component of the nail dystrophy and that the nail may still look bad due to the psoriasis.

Figure 12. Toenail fungal infection.

The other common presentation of a fungal infection of the toenails is a patient who is neither concerned nor aware of the significance of the nail disease. Such a patient may present with, for example, chronic tinea of one foot or both feet, recurrent tinea of the inguinal folds or hair-bearing areas of the leg and buttocks, or recurrent cellulitis (with or without chronic venous insufficiency). He or she does not complain of nail disease, but hyperkeratotic or discoloured dystrophic toenails are apparent on examination (Figure 12) and clearly contributing to the recurrence of glabrous tinea (Figure 7) or secondary bacterial infections. In this situation, it is important to scrape and clip the involved toenails for KOH microscopy and culture and to treat this chronic source of dermatophyte infection.

If there are problems of recurrent glabrous skin fungal infections or recurrent cellulitis with the portal of entry being the maceration between the toes, it is important to consider more seriously the use of oral antifungal agents to treat the nail source of the recurrent infection. The first choice would be oral terbinafine. If significant side effects occur it would be necessary to consider oral itraconazole, provided that the patient is not taking any contraindicated drugs. Other situations in which toenail involvement may need to be treated include patients with diabetes or those who are immunosuppressed.

A variation on this presentation is a child who presents with tinea of the face, body, limbs or toenail; *Trichophyton rubrum* or *Trichophyton mentagrophytes* is grown on specimens taken for fungal culture. These two species of dermatophyte commonly infect adults' feet. In addition to treating the child, it is worthwhile checking the adults in the family for toenail tinea and treating this source.

Summary

There are many causes of dystrophy affecting the nails. Clinical symptoms and signs of the involved nails and other cutaneous lesions may help with the differential diagnosis. If a single nail is involved and nail plate destruction is evident, a biopsy will be needed to exclude a cutaneous malignancy.

A fungal infection may occur as a secondary phenomenon in nails that are dystrophic due to another cause. Many specimens taken for microscopy and culture give false negative results – reasons include poor sampling and use of topical antifungal preparations prior to testing.

All the potential side effects and drug interactions need to be considered in the decision to treat the nail fungus infection with systemic therapies, particularly if the problem is merely cosmetic. When there is significant recurrent pathology of the glabrous skin with fungal infection or recurrent cellulitis, the need to treat is more significant. MT

References

1. Crawford F, Hart R, Bell-Syer S, Torgerson D, Young P, Russell I. Topical treatments for fungal infections of the skin and nails of the foot. Cochrane Database Syst Rev 2000; (2): CD001434.

2. Crawford F, Young P, Godfrey C, et al. Oral treatments for toenail onychomycosis: a systematic review. Arch Dermatol 2002; 138: 811-816.