Chapter 14
Mimickers

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Key Features
- Various nail disorders causing subungual hyperkeratosis and/or onycholysis can mimic onychomycosis.
- Diagnosis of onychomycosis requires laboratory studies.
- Differential diagnosis depends on the clinical type of onychomycosis

Introduction

Onychomycosis is the diagnosis for onychodystrophic nails about 50 % of the time [1]. However, there are a variety of other etiologies that may be causing the onychodystrophic nails. These other conditions may mimic onychomycosis in their presentations and must be excluded before initiating antifungal treatment.

Mimickers for onychomycosis include inflammatory, infective, and neoplastic nail disorders, as well as nail manifestations of systemic diseases. This chapter will discuss differential diagnoses according to the clinical type of onychomycosis.

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Distal Subungual Onychomycosis

Differential diagnosis includes nail diseases that cause subungual hyperkeratosis and/or onycholysis.

Subungual hyperkeratosis and onycholysis	Psoriasis
	Contact dermatitis
	Nail bed lichen planus
Onycholysis	Traumas
	Yellow nail syndrome
	Nail bed tumors (warts, exostosis, squamous cell carcinoma, melanoma)
Subungual hyperkeratosis	Pachyonychia congenita

Nail Psoriasis

Epidemiology

Psoriasis of the nails is the most common mimicker of onychomycosis [2]. Psoriasis involves the nails in 80–90 % of patients. Only 5 % of psoriasis cases will have isolated involvement of the nails [1].

Clinical Features

Nail psoriasis presents clinically with pitting, onycholysis with erythematous border, salmon patches, subungual hyperkeratosis, and splinter hemorrhages, among other nail abnormalities [3].

The most common change seen in nail psoriasis is pitting, in which small depressions of less than 1 millimeter diameter are seen on the surface of the nail plate, due to the presence of parakeratotic cells [3]. This is the result of psoriatic lesions, which consist of clusters of parakeratotic cells in the proximal nail matrix. These clusters disrupt normal keratinization and eventually are removed as the nail grows outward, leaving depressions on the nail surface (Fig. 14.1).

A salmon-colored patch may be seen beneath the nail plate, resembling an oil drop. The red-yellow discoloration is the result of parakeratotic lesions within the nail bed that are visible through the overlying nail plate. This “oil drop” sign is the most diagnostic finding of nail psoriasis. Onycholysis occurs when the parakeratotic lesions involve the hyponychium. Air enters the space between the nail bed and overlying nail plate and may cause white discoloration [1]. Psoriatic onycholysis is typically surrounded by an erythematous border.

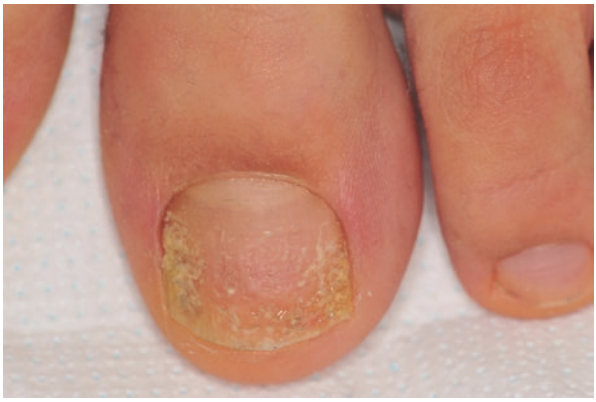

Fig. 14.1 Nail psoriasis. The presence of pitting suggests diagnosis

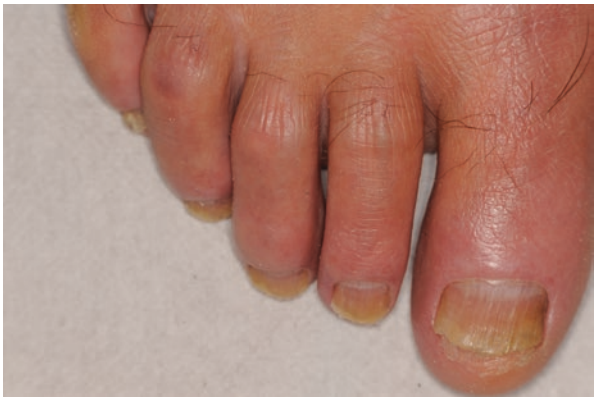

Fig. 14.2 Nail psoriasis presenting with subungual hyperkeratosis, onycholysis, and yellow discoloration

Subungual hyperkeratosis results from deposition and accumulation of desquamated cells underneath the nail plate. This leads to detachment of the nail plate from the nail bed. The degree of this detachment depends upon the level of psoriatic activity present. Subungual hyperkeratosis in nail psoriasis is typically characterized by a silvery-white discoloration as opposed to the typical yellow, greasy appearance seen in onychomycosis, but this is not always the case [1, 4] (Fig. 14.2).

Splinter hemorrhages are less commonly seen and appear as linear, thin, deep, red to black lines in the distal nail. These occur in the dermis of the nail bed, when small capillaries rupture into the linearly oriented epidermal-dermal ridges. Splinter hemorrhages are not only associated with psoriasis, as they can present in a number of other medical conditions, particularly trauma, as observed in 20 % of cases. They are also seen in onychomycosis and even in healthy individuals with inherently delicate capillaries [4].

Leukonychia, which represents white areas of the nail due to parakeratotic foci within the nail plate, can also be a sign of psoriasis [5]. When psoriasis affects the whole matrix, the nail is distorted, rough, and friable [3, 4].

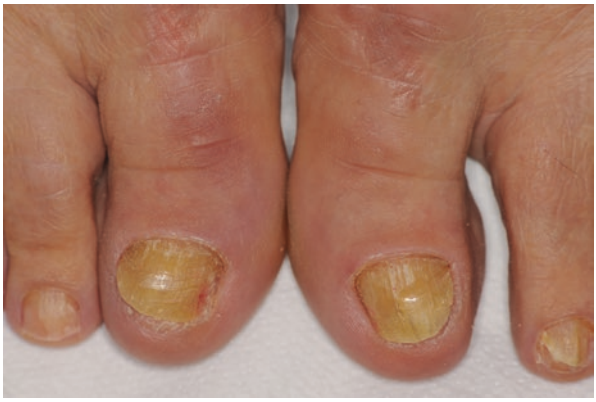

Fig. 14.3 Nail bed lichen planus. Nails are thickened and *yellow* in color; note onychorrhexis that suggests correct diagnosis

Lichen Planus

Epidemiology

Lichen planus is a chronic inflammatory disease with unknown etiology that affects the skin, hair, nails, and mucous membranes [1, 6]. The prevalence of lichen planus is not known, but is estimated to be less than 1 %. It affects women and men equally. It can occur at any age, but the majority of cases are in patients between 30 and 60 years old [7]. Lichen planus involves the nails in about 10 % of cases and can be limited to the nails only [8].

Clinical Features

Lichen planus most commonly involves the nail matrix causing longitudinal grooves and fissures, as well as progressive thinning and distal splitting of the nail plate [8]. Nail matrix destruction causes dorsal pterygium, in which the proximal nail fold adheres to the nail bed [1, 6, 9].

However, lichen planus can also affect the nail bed causing subungual hyperkeratosis and onycholysis. In the toenails it often causes yellow discoloration and thickening (yellow nail syndrome-like presentations) (Fig. 14.3). In general, patients also present signs of nail matrix involvement that suggest correct diagnosis.

Subungual Tumors

Warts

Epidemiology

Periungual warts are most commonly seen in children and teenagers, occurring most frequently in those ranging from 12 to 16 years old. There is increased incidence in those who bite their nails, who suck their fingers, and who work in a wet environment. Often, warts disappear spontaneously [10].

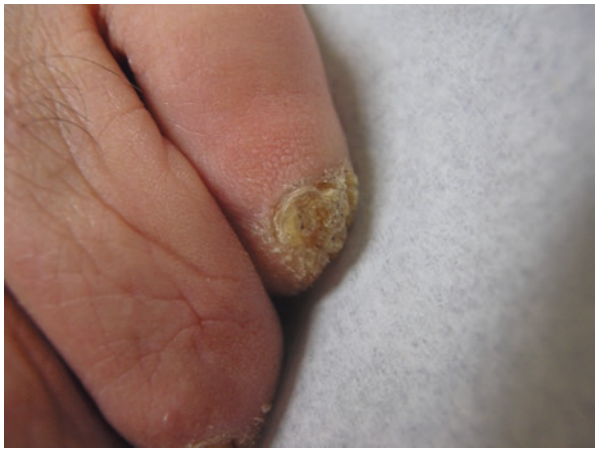

Fig. 14.4 Periungual wart

Clinical Features

Periungual warts are usually caused by HPV genotypes 1, 2, and 4. They affect fingernails more often than toenails and appear as hyperkeratotic papules with a rough surface (Fig. 14.4). Pathologically, they are characterized as having sharply demarcated hyperplasia with acanthosis, papillomatosis, and hyperkeratosis with areas of parakeratosis [10].

Initially, the warts are small in size, shiny, smooth, and translucent. Weeks to months later, they grow in size and appear rough, dirty, brownish black in color, and horny [11].

When located in the proximal nail fold, warts produce periungual hyperkeratosis forming a hyperkeratotic cuticle. Subungual warts raise the nail plate causing onycholysis and appear as a subungual nodular lesions. They may also produce a longitudinal band of onycholysis with splinter hemorrhages due to linear growth underneath the nail plate. Warts in the hyponychium of the toenails may cause distal thickening.

Warts do not affect the nail matrix, but can cause damage to it due to compression, which can cause nail plate ridging and grooving [10]. They may become fissured, inflamed, and tender and often recur after treatment [11].

Exostosis

Epidemiology

Subungual exostosis is a rare, benign osteocartilaginous tumor affecting the distal phalanx of the digits, usually the toes [12]. It presents more frequently in females and most often in the second decade of life. About one-third of patients report a history of trauma or infection at the site [13].

Clinical Features

Patients commonly present with months of pain, erythema, and onycholysis [1, 12]. It most often affects the toenails, with about 70–80 % of cases overall affecting the hallux [14].

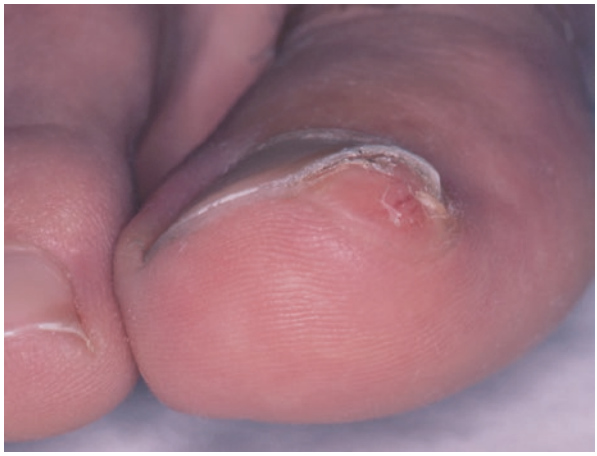

Fig. 14.5 Subungual exostosis

Examination shows a firm nodule with a hyperkeratotic and smooth surface (Fig. 14.5). The lesion is located at the distal end of the nail plate, away from the epiphyseal line. It is made of trabecular bone and is capped with fibrocartilage [12].

Squamous Cell Carcinoma

Epidemiology

Squamous cell carcinoma of the nail is rare [15]. It is most common in the fifth and sixth decades of life and tends to have a male predominance [16].

The etiology of subungual squamous cell carcinoma is unclear, although repeated trauma, chronic infection, radiation, tar, arsenic exposure, UV radiation, immunosuppression, and HPV infection may each play a role. HPV infection is particularly relevant as it is present in 60–90 % of cases [15].

Clinical Features

Subungual squamous cell carcinoma most frequently presents on the hands rather than the feet [17]. It most often involves only one digit, with the thumb and hallux being the most common [15]. The right index and middle fingers are also commonly affected [18].

Patients most commonly present with a wartlike appearance of the nail bed with nail dystrophy [15]. Nail pigmentation with longitudinal melanonychia is common (Fig. 14.6) [18].

Other clinical features include subungual hyperkeratosis, onycholysis, oozing, nail plate destruction, paronychia, leukonychia, and longitudinal erythronychia [18]. Bleeding along with nodules and ulcers may also be present [15].

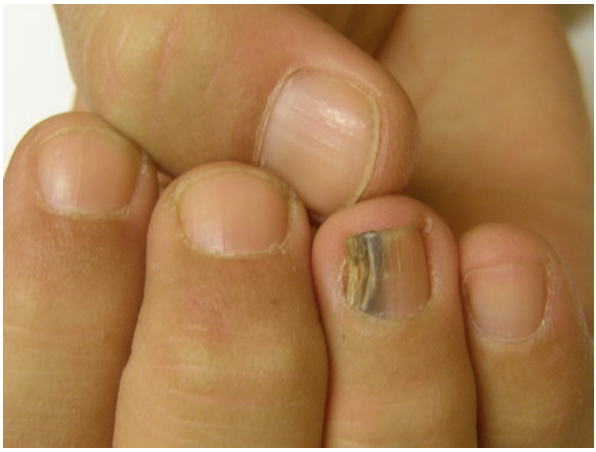

Fig. 14.6 Squamous cell carcinoma presenting with longitudinal melanonychia

Subungual Melanoma

Epidemiology

Nail melanoma is not common, as it accounts for only about 1–3 % of cutaneous melanomas diagnosed in the general population [19, 20]. Nail melanomas are seen more often in patients 50–70 years old and more often in men than women [19, 20]. Darker-skinned individuals are more commonly affected with this subtype of melanoma. Up to 75 % of cutaneous melanomas are localized in the nail in Africans, 10 % in Japanese, and 25 % in Chinese populations [20].

Clinical Features

Nail melanomas originate either from the nail matrix, or the nail bed (subungual melanomas), and may involve other parts of the nail unit such as the proximal nail fold and hyponychium. Nail matrix melanoma presents as bands of longitudinal brown-black discolorations of the nail plate (longitudinal melanonychia) [20]. The pigmented band is usually wider than 3 mm and has dishomogeneous color and blurred lateral margins (Fig. 14.7) [19, 20]. Nail bed melanoma appears as a pigmented or nonpigmented subungual nodule that initially causes nail plate detachment. It gradually enlarges, eventually leading to nail plate destruction [19]. Ulceration, pain, inflammation, discharge, and surrounding discoloration are common [20].

Hutchinson sign is a characteristic feature of invasive subungual melanoma. It is defined as extension of the dark pigment into the lateral or proximal periungual folds [1].

Nail melanomas are more often found in the hands than in the feet and most commonly in the thumb and hallux [19]. Although UV radiation is a well-known risk

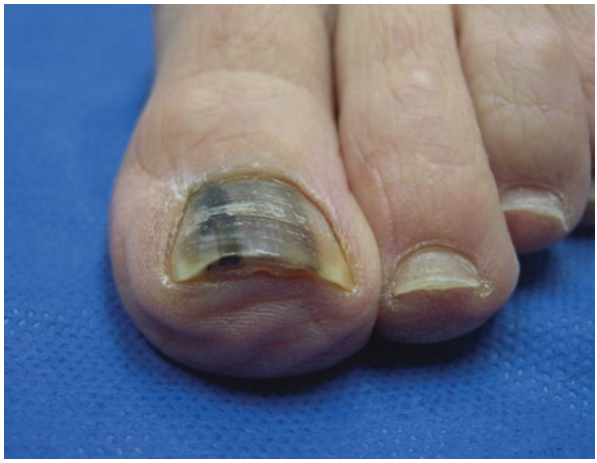

Fig. 14.7 Nail matrix melanoma presenting with longitudinal melanonychia

factor for cutaneous melanoma, it is unable to penetrate the nail plate and therefore is not a risk factor for subungual melanoma [19]. Instead, direct trauma to the nail is frequently reported although there is lack of evidence to form a direct correlation [20].

Contact Dermatitis

Epidemiology

Contact dermatitis can be allergic or irritant and causes inflammation of the skin due to chemical damage. It can occur at any age and is more prevalent in women and manual laborers [1].

Clinical Features

Contact dermatitis frequently affects the nail bed as chemicals penetrate through the thin onychodermal band causing subungual inflammation with onycholysis and subungual hyperkeratosis. This can be very severe in patients with contact allergy to acrylic nails (Fig. 14.8). Splinter hemorrhages are also common.

Diagnosis is suggested by the presence of periungual erythema and scaling as well as Beau's lines.

Traumatic Onycholysis

Epidemiology

Trauma of the nail unit is a common injury that can mimic onychomycosis. Trauma can be due to footwear, mechanical injury, or athletics. Traumatic nail lesions can be observed in patients of any race, sex, or age and is very commonly misdiagnosed and treated as onychomycosis.

Fig. 14.8 Contact dermatitis due to acrylic nails

Clinical Features

Signs of trauma include onycholysis, subungual hyperkeratosis, abnormalities of the nail plate, changes in the hyponychium, ingrown nails, paronychia, and onychomadesis [1]. Traumatic onycholysis usually affects the big toes and is common in athletes and in women wearing high-heel shoes. It affects the lateral aspect of the toenail when caused by overlapping of the second toe or the distal nail [21] (Fig. 14.9).

It may frequently be colonized by microorganisms that produce pigments mimicking onychomycosis [2]. At dermoscopy, the proximal border of the onycholytic area is sharp.

Subungual hematoma may also occur secondary to trauma. This would produce a dark reddish-black subungual discoloration (Fig. 14.10). This discoloration would move forward and become more blue in color as the nail grows outward. Distal onycholysis and spontaneous avulsion may also occur with subungual hematoma [22]

Pachyonychia Congenita

Epidemiology

Pachyonychia congenita is a rare genetic skin disease, due to a defect in one of four keratin genes [23]. There are only an estimated 5000–10,000 cases of pachyonychia congenita reported worldwide. It affects males and females equally and has a large geographic distribution [23].

Clinical Features

Most patients with pachyonychia congenita will present with symptoms at birth or within 1 year. Three clinical features that are present in most patients regardless of mutation subtype are thickened toenails, plantar keratoderma, and plantar pain [23].

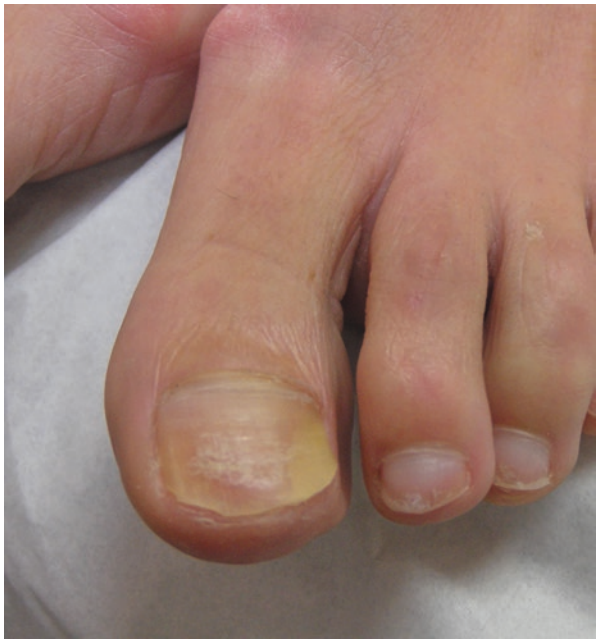

Fig. 14.9 Traumatic onycholysis due to overlapping of the second toe over the first toenail

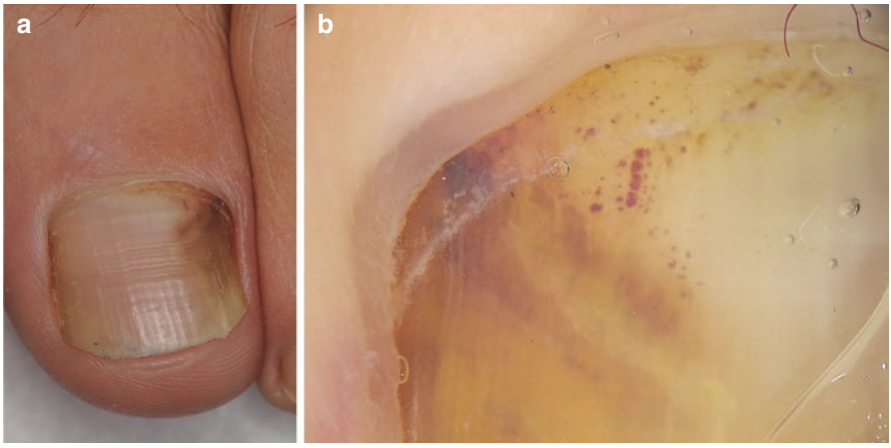

Fig. 14.10 (**a**) Traumatic onycholysis and subungual hematoma. (**b**) Dermoscopic examination showing typical red round spots due to blood extravasation

The nails show subungual hyperkeratosis in about 90–98 % of cases [1, 24]. They are very thick and develop large horns that require matrix removal in order to halt their growth [1]. Thickened toenails are the most frequently reported symptom, with the majority of the toenails being affected and in most cases all ten. Patients often file the nails to reduce the thickening (Fig. 14.11). Fingernails are less commonly affected than toenails, but may present with the same clinical features [23].

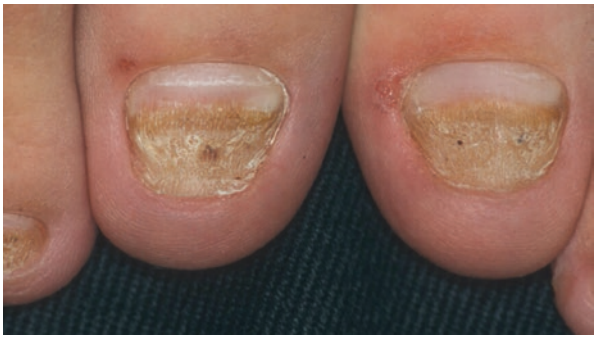

Fig. 14.11 Pachyonychia congenita affecting the toenails

Nails may also show yellowish-brown discoloration and upward angulation of the free edge of the nail plate secondary to the progressive thickening [25]. Nails may also show premature termination of the nail plate with an exposed distal fingertip [26].

Onycholysis Due to Thyroid Disease

Epidemiology

Thyroid disease is a common disorder and can be divided into two groups: hyperthyroidism and hypothyroidism. Both types can be caused by autoimmunity or iodine deficiency.

Clinical Features

Both hyperthyroidism and hypothyroidism can cause onycholysis.

Onycholysis due to hyperthyroidism is also known as Plummer's nails [27]. The hyponychium appears dirty, and brown discoloration of the nails may be seen. All of the nails of the fingers and toes are usually affected, but the fourth finger is usually the first one to show symptoms, particularly onycholysis [1].

Yellow Nail Syndrome

Epidemiology

Yellow nail syndrome is a rare disorder that presents nail abnormalities in association with lymphedema or chronic respiratory disease. Onset of yellow nail syndrome is typically seen in adulthood, most often during the fourth and sixth decade of life [28]. . Men and women are equally affected [29, 30].

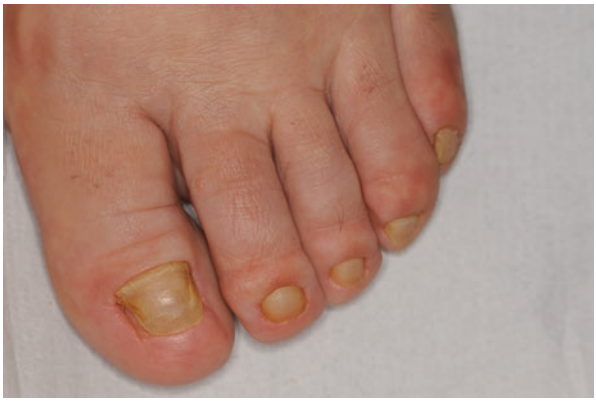

Fig. 14.12 Yellow nail syndrome

Clinical Features

Yellow nail syndrome is characterized by a triad of clinical features: yellow nails, lymphedema, and chronic respiratory involvement (pleural effusion, bronchiectasis, sinus infection, chronic cough, and chronic lung infections). Two of these features must be present in order to make a diagnosis of yellow nail syndrome [1, 28].

Nails are primarily affected with yellow discoloration and arrested or abnormally slow growth. The cuticle is absent and the nails are overcurved, and onycholysis is common (Fig. 14.12) [31]. The nail changes are reversible and might resolve spontaneously, with control of the respiratory symptoms or of the lymphedema [29, 30].

Drug-Induced Onycholysis

Epidemiology

Cutaneous drug reactions account for 10–30 % of all adverse drug reactions. Women and men are affected equally, and the possibility of cutaneous adverse drug reactions tends to increase with age [32].

The most popular drugs causing nail abnormalities include tetracyclines, psoralens, quinolones, and taxanes [33].

Clinical Features

Drug-induced nail changes usually affect most or all of the nails, on both the hands and feet. Nail changes are frequently reversible upon drug withdrawal, except discoloration which can remain for years.

Tetracyclines rarely cause photo-onycholysis, which occurs after drug ingestion and exposure to UV light. Photo-onycholysis causes nail plate detachment with

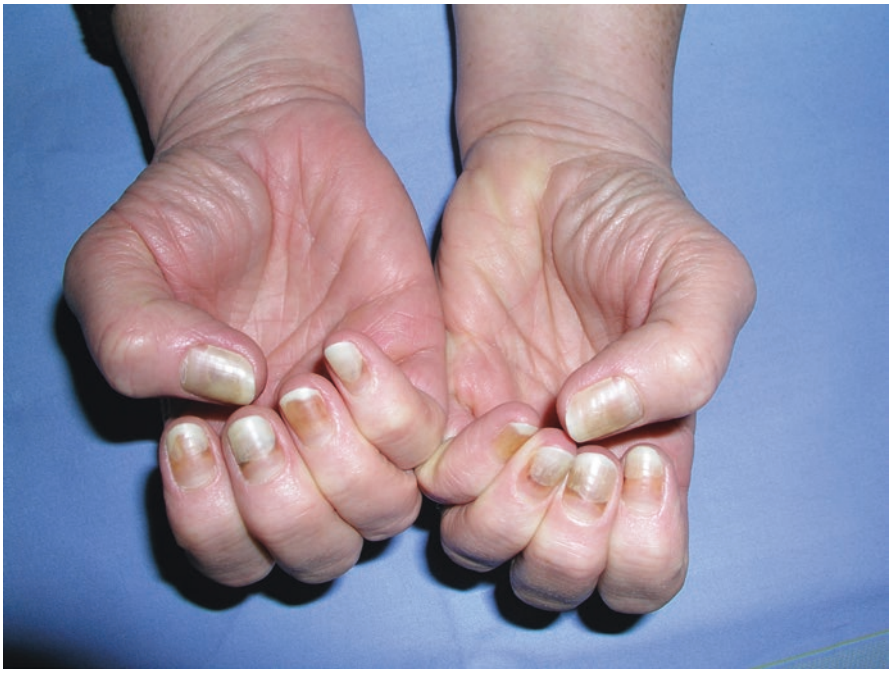

Fig. 14.13 Hemorrhagic onycholysis due to taxanes

subungual hemorrhages. It most often affects the fingernails meanwhile sparing the thumb and will involve the toenails if they are exposed to the sun. Pain may be present in some patients, as well as a convex-shaped nail. It usually appears after 2 or 3 weeks of taking the drug, and symptoms may occur even after discontinuation of the drug. Other drugs that are known to cause photo-onycholysis are psoralens, quinolones, chloramphenicol, and NSAIDs [1, 34].

Onycholysis can result from damage to the nail bed or formation of hemorrhagic bulla due to drug reactions. The hemorrhagic bulla can be painful, but fortunately the nail resolves upon drug withdrawal. Drugs that can cause this condition include psoralens, retinoids, and chemotherapeutic drugs [33].

Taxanes commonly cause painful hemorrhagic onycholysis with subungual exudation (Fig. 14.13).

Proximal Subungual Onychomycosis

The differential diagnosis includes diseases that cause true leukonychia and proximal onycholysis.

Fig. 14.14 Transverse leukonychia due to manicure

True Leukonychia

True leukonychia is caused by abnormal nail plate maturation with the presence of parakeratotic cells within the nail plate. Traumas and hereditary conditions can be responsible. Overzealous manicures cause transverse leukonychia that might resemble recurrent bands of proximal subungual onychomycosis (Fig. 14.14).

Proximal Onycholysis

This can be a consequence of trauma. The proximal nail is white because of the presence of air, but the color is not opaque white as it is in leukonychia from proximal subungual onychomycosis.

White Subungual Onychomycosis

Pseudo-leukonychia

Brittle nails due to continuous wearing of nail polish may present with white patches of pseudo-leukonychia due to superficial keratin degranulation that looks similar to white superficial onychomycosis (Fig. 14.15). However, keratin degranulation is usually seen in fingernails, and it is important to keep in mind that this type of onychomycosis is exclusively seen in toenails.

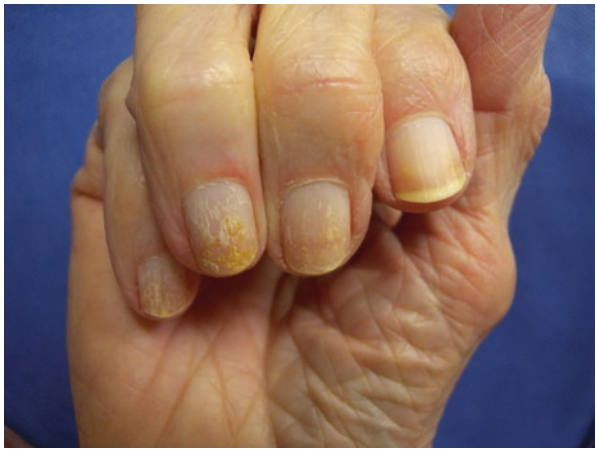

Fig. 14.15 Pseudo-leukonychia due to repeated use of nail polish

Diagnostic Clues

In general, onychomycosis is unlikely when all toenails are affected, fingernails of both hands are affected, and subungual nodules are present.

Psoriasis: look for pitting/salmon patches, skin/scalp involvement, and joint enlargement/pain.

Nail bed lichen planus: look for signs of nail matrix involvement.

Nail melanoma: utilize ABCDEF guidelines and brown/black color with irregular lines at dermoscopy (Table 14.1).

Contact dermatitis: usually fingernails, periungual skin frequently affected.

Table 14.1 ABCDEF guidelines for diagnosis of subungual melanoma

A	*A*ge: peaks at 50–70 years old Race: *A*frican-*A*merican, Native *A*merican, *A*sian
B	*B*and *B*rown-*b*lack pigment *B*readth of band > 3 mm *B*order is irregular/blurred
C	*C*hange: in size and growth rate Lack of *c*hange: failure of nail dystrophy to improve with treatment
D	*D*ominant hand *D*igit involved: thumb > hallux > index finger Single digit > multiple digits affected
E	*E*xtension of pigment discoloration (Hutchinson sign)
F	*F*amily (or personal) history of melanoma

Traumatic onycholysis: look for podiatric abnormalities including hallux valgus/overlapping of second toe on first toe (Greek foot)/round dark spots corresponding to hematoma at dermoscopy.

Pachyonychia congenita: onset during early infancy, nail thickening without onycholysis, and severe pain.

Onycholysis in thyroid disease: several fingernails commonly affected.

Yellow nail syndrome: arrested nail growth, most fingernails usually affected.

Drug-induced onycholysis: all nails usually involved, often hemorrhagic.

True leukonychia: many nails involved, cuticle damaged when caused by traumas.

Pseudo-leukonychia: usually fingernails (not affected by WSO), staining from nail polish commonly associated.

Summary for the Clinician

Fungal infection leads to onychodystrophic nails only about 50 % of the time [1]. The other 50 % of onychodystrophic nails may be attributed to the clinical mimickers of onychomycosis, all outlined above. It is important for the clinician to be aware of these mimickers when diagnosing the patient and selecting treatments, as the various conditions require different treatments.

Onychodystrophies can have significant effects on patients' emotional, social, and occupational behaviors because of their esthetic effects or pain [2]. Therefore, misdiagnosis can prolong these effects, and the infection may worsen, representing the need for correct diagnosis in a timely manner.

Clinical Pearls

It is not onychomycosis when:

- All nails are involved.
- All fingernails are involved.
- Onycholysis is not associated with subungual hyperkeratosis.
- Proximal border of onycholysis is sharp.

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