When all you have is a dermatoscope—start looking at the nails

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ABSTRACT

Pigmented and non-pigmented nail alterations are a frequent challenge for dermatologists. A profound knowledge of clinical and dermatoscopic features of nail disorders is crucial because a range of differential diagnoses and even potentially life-threatening diseases are possible underlying causes.

Nail matrix melanocytes of unaffected individuals are in a dormant state, and, therefore, fingernails and toenails physiologically are non-pigmented. The formation of continuous, longitudinal pigmented streaks (longitudinal melanonychia) may either be caused by a benign activation of matrix melanocytes (e.g., as a result of trauma, inflammation, or adverse drug reactions) or by a true melanocytic proliferation (e.g., in a nevus or melanoma). In general, non-continuous nail alterations, affecting only limited parts of the nail apparatus, are most frequently of non-melanocytic origin. Important and common differential diagnoses in these cases are subungual hemorrhage or onychomycosis. In addition, foreign bodies, bacterial infections, traumatic injuries, or artificial discolorations of the nail unit may less frequently cause non-continuous nail alterations. Many systemic diseases that may also show involvement of the nails (e.g., psoriasis, atopic dermatitis, lichen planus, alopecia areata) tend to induce alterations in numerous if not all nails of the hands and feet. A similar extensive and generalized alteration of nails has been reported after treatment with a number of systemic drugs, especially antibiotics and cytotstatics. Benign or malignant neoplasms that may also affect the nail unit include glomus tumor, Bowen’s disease, squamous cell carcinoma, and rare collision tumors. This review aims to assist clinicians in correctly evaluating and diagnosing nail disorders with the help of dermatoscopy.
Introduction

The clinical and dermatoscopic evaluation of nail alterations is often a diagnostic challenge for dermatologists in their daily practice. Regarding the variety of different patterns, it is helpful to follow a standardized diagnostic algorithm (Figure 1A) and to memorize the dermatoscopic features of the most frequent nail disorders as depicted by the schematic icons in Figure 1B [1]. In agreement with the evaluation of pigmented lesions elsewhere on the skin, a multi-step diagnostic procedure has proven to be successful [2]. A first step is dedicated to the differentiation of a melanocytic origin (longitudinal melanonychia) from a non-melanocytic origin of the nail pigmentation (non-continuous discoloration).

For all non-melanocytic nail disorders, a diagnosis should be made based on typical dermatoscopic criteria (Figure 1B, e.g., subungual hematoma). In most of these cases, the clinical picture and dermatoscopic criteria will lead to a final diagnosis and further diagnostic measures will not be necessary [3-5]. However, a follow-up examination with comparison of clinical/dermatoscopic findings to baseline images may be useful to safely confirm the initial diagnosis [1]. In case of a longitudinal melanonychia, the distinction between a benign activation of melanocytes (Figure 1B, lentigo, mostly grayish background with longitudinal homogeneous gray lines) and a true melanocytic proliferation ensues in a second step. If a melanocytic proliferation is present, the differentiation between nevus and melanoma is required (Figure 1B) [6,7]. The confident diagnosis of melanoma in situ or early invasive melanoma by clinical appearance and dermatoscopy may especially cause difficulties, and a biopsy of the nail matrix should be performed in any case of doubt [8]. The solid surface of the nail unit with its convexities and concavities may prevent the exact optical attachment of the dermoscope to the nail by immersion oil or disinfectant agents. We recommend the use of ultrasound gel as a contact medium or the use of dermatoscopes with polarized light in the nail region.
Non-continuous (non-melanocytic) nail alterations

Onychomycosis

The most common clinical form of onychomycosis shows a distolateral pattern that often involves the nails of the first and/or fifth toe. Dermatoscopic examination typically reveals: (i) a whitish discoloration of the nail, (ii) superimposed longitudinal parallel striation, and (iii) jagged proximal edges with spikes (Figure 2A, B). Moreover, small splinter hemorrhages and various nail discolorations (chromonychia) with green, yellow or brown colors may occur [5,9]. Of note, an intense green color of the nail plate severely affected by a mycotic infection often indicates a secondary infection with *Pseudomonas* species (Figure 3A, B). After a clinical and dermatoscopic examination the causative dermatophytes (mostly *Trichophyton rubrum*, *Epidermophyton* or *Microsporum* species) may be differentiated by cultural techniques.

Subungual hemorrhage/subungual hematoma

In addition to the subcorneal hemorrhage, the subungual hemorrhage (also called subungual hematoma) is one of the most frequent differential diagnoses of acral pigmented lesions. A detailed documentation of the lesion history should give first evidences for the causes of the subungual hemorrhage (e.g., trauma, anticoagulation). It usually appears as a reddish-blue to blue-black pigmentation that does not longitudinally involve the whole nail. The characteristic dermatoscopic findings of subungual hemorrhage are homogeneous or globular patterns, streaks, peripheral fading and also periangual hemorrhages of adjacent skin [10]. Moreover, small, globular blood dots directed towards the distal end of the nail plate are a highly characteristic dermatoscopic feature that often leads to the correct diagnosis (Figure 4A-C). Importantly, a proximal subungual hematoma may be visible through the widely transparent cuticula; this should not be confused with the (micro-) Hutchinson sign characterizing a subungual melanoma. Subungual hemorrhage will continuously be transferred towards the distal edge of the nail at the speed of the nail growth. Sequential digital dermatoscopy follow-up may confidently be used to document the progressive “growing-out” of a subungual hemorrhage. Any subungual hemorrhage that persists and eventually forms a longitudinal pigmentation involving the complete nail apparatus requires further diagnostic procedures including biopsy.

Systemic diseases involving the nail unit

Nail psoriasis with pitted and thickened nails, onycholysis and psoriatic crumbling of the nail plate can easily be inspected with the naked eye. Dermatoscopy can be helpful for the diagnosis when the typical clinical features are absent or subtle. In patients with psoriatic onycholysis, dermatoscopy helps to visualize the inflammatory, erythematous border surrounding the distal edge of the detached nail plate [4]. The accuracy of the evaluation of psoriatic splinter hemorrhages and subungual hyper-/parakeratosis is increased. Similar to nail psoriasis, patients with atopic diathesis or manifest atopic dermatitis may have pitted nails without further characteristics (Figure 5A, B).

Onychopapilloma and subungual viral wart

Onychopapilloma is a benign neoplasms, that originates from the distal nail matrix and/or the nail bed [11,12]. It typically presents with longitudinal leukonychia or longitudinal erythronychia that does not continuously involve the whole nail, but that leaves an unaffected interval at the proximal nail matrix. Importantly, cases of onychopapilloma presenting as longitudinal melanonychia of grayish color have been
reported [13]. The dermatoscopic view from the free distal margin of the nail plate typically reveals a wedge-shaped hyperkeratotic notch (Figure 6A-D).

The diagnosis of acral viral warts is often easily made by a clinical inspection. However, dermatoscopic examination may be useful for the diagnosis of small, subclinical or subungual warts or for the assessment of the therapeutic success after treatment. A yellowish, rough-verrucous surface with multiple, brown-red dots and/or streaks, which correspond to dilated capillaries and small hemorrhages are characteristic dermatoscopic criteria [14,15]. A decrease of the capillary density within viral warts is often observed in lesions responding to treatment.

Artifacts and foreign bodies of the nail unit

Artificial changes of the nail unit occasionally arise and may be quite worrisome for patients. In the summer, moist leather of shoes may cause irregular dark-brown discolorations of some toenails, which can easily be removed mechanically (Figure 7A-E). Additionally, the use of self-tanning lotions or tanning showers may lead to a homogeneous yellow-brownish discoloration of all nails (Figure 8A, B). Occasionally, foreign body injuries of the nail unit, accompanied by subungual hemorrhage, subungual serum- and air-inclusions may be observed, especially in patients walking barefoot (Figure 9A, B).

Other neoplasms of the nail unit

Glomus tumor

Glomus tumors represent approximately 1 to 5% of the soft tissue tumors of the hand. They are a subtype of benign venous malformations characterized by rows of glomus cells that surround distorted, thin-walled vascular channels.
Glomus tumors of the nail unit are painful, vascular proliferations with an increased sensitivity to cold temperatures and pressure. They arise from myoarterial structures (Hoyer-Grosser's organs) of the nail unit [16]. Nearly two-thirds of glomus tumors are localized on the hands, particularly the subungual region. In addition to numerous clinical tests that examine the painfulness and the increased sensitivity to cold, the use of dermatoscopy helps to localize the tumors and to visualize the vascular pattern of the lesion. Furthermore, the use of dermatoscopy facilitates the delimitation of surgical margins before treatment (Figure 10A, B) [16].

Bowen's disease and squamous cell carcinoma

In the aging population tumors with increasing incidences (Bowen's disease, squamous cell carcinoma) may also arise in less common localizations including the nail bed or the skin below the distal nail plate. The clinical presentation of these tumors is often atypical and they are usually non-pigmented; therefore, their diagnosis is often missed or delayed. Moreover, these tumors may be misinterpreted as other benign conditions such as verruca vulgaris, onychomycosis or trauma-induced nail dystrophy [14]. Dermatoscopically, the characteristic pattern of pigmented Bowen's disease with its typical brownish dots along imaginary lines can frequently be observed (Figure 11A, B) [17]. In contrast, non-pigmented Bowen's disease or squamous cell carcinoma may often show dot-like to glomerular vessels clustering in groups (up to vascular polymorphism) [18]. The potential risk of misdiagnosing subungual bowenoid squamous cell carcinoma as verruca vulgaris is exemplified in Figure 12 (Figure 12A-C) and 13 (Figure 13A, B).

Collision tumors (squamomelanocytic tumor)

A collision tumor is a cutaneous proliferation composed of closely intermingled cells of two independent tumor entities at the same location, e.g., of a melanoma and a squamous cell carcinoma. A squamomelanocytic tumor is such a collision tumor that mostly occurs in sun-exposed skin of the face and neck area of older patients [19,20]. Recently, a first squamomelanocytic tumor of the nail unit has been reported [21]. The clinical and dermatoscopic examination revealed an advanced dystrophy of the nail plate with brown to slate-gray periungual pigmentation (corresponding to invasive melanocytes of the melanoma) and several keratin cysts of the...
adjacent skin (corresponding to areas of keratinization of the squamous cell carcinoma) (Figure 14 A, B).

**Continuous (melanocytic) nail alterations (longitudinal melanonychia)**

In contrast to the direct inspection of a localized melanocytic proliferation in case of a nevus or melanoma on the skin, the site of melanocytic proliferation within the nail matrix or proximal nail bed is not accessible for a direct dermatoscopic inspection. This means that the examination of longitudinal melanonychia is limited to the inspection of pigment that was deposited in the nail plate weeks to months earlier [22]. Continuous longitudinal pigmented bands within the nail plate may represent melanocytic nevus, lentigo, racial/ethnic melanonychia, drug-induced hyperpigmentation, or malignant melanoma [6]. Benign longitudinal melanonychia is rare in Caucasians—only 1.4% of the population is affected. Interestingly, the thumb, followed by the great toe and the index are involved most frequently [6].

**Drug-induced melanocytic activation**

A range of drugs has been associated with the formation of nail alterations. However, only a few drugs are regularly responsible for toxic effects on the nail matrix, the nail bed or the periungual skin [23]. These drugs predominantly include retinoids and chemotherapeutics like docetaxel (taxotere) (Figure 15A, B) [24]. Besides diffuse dark pigmentation of all nails and Beau’s lines (lines appearing as horizontal and deep grooves of all fingernails), subungual hemorrhage, orange discolorations, acute painful paronychias, onycholysis, subungual hyperkeratosis and transverse loss of the nail plate are described for docetaxel, in which the type of nail alteration is related to the number of administered cycles. Additionally, minocycline was repeatedly associated with gray-blue longitudinal melanonychias that are clinically very similar to ethnic subungual lentigo [25,26]. Pigmentations usually occur after prolonged minocycline treatment, however, not always in a dose-dependent manner and mostly after treatment intervals of more than a few years, and may coincide with other pigmented sites.
Ethnic-type nail pigmentation (nevoid lentigo of the nail unit)

The ethnic subungual lentigo predominantly occurs in humans with a darker skin type categorized according to Fitzpatrick skin classification (e.g., Indian skin type, skin type V). Multiple nails are frequently affected and the color is homogeneous gray-brown. The thin longitudinal lines that might be discriminated within the pigmented band are regular in their coloration, thickness and spacing (Figure 16A, B) [7,8]. The lateral margin of pigmentation is often diffuse. Occasionally, the pigmented band of a subungual ethical lentigo is very subtle and pale and therefore may be difficult to separate from the uninvolved nail-plate in a clinical-dermatoscopic examination.

Benign nevus of the nail unit

Characteristics for subungual benign nevi are their appearance in children and young adults and their regular pattern of the longitudinal lines. The width of the pigmented band of subungual nevi is rather low (normally ≤3 mm) and regular in thickness and spacing of striation. The color of different subungual nevi varies from light brown to dark brown to black [3]. The pigmentation within one lesion is mostly homogeneous or is composed of evenly distributed thinner lines of the same color (Figure 17A, B). Congenital acral nevi may also involve an increased melanocytic pigmentation of the nail unit (Figure 18A, B). Many congenital nevi at acral sites may clinically look suspicious at first sight and should thoroughly be inspected by using dermatoscopy. The double dotted parallel furrow pattern depicted in Figure 18 was described as a typical acral volar skin pattern in younger individuals [27]. Over the course of time when examined by sequential digital dermatoscopy the degree of pigmentation of the longitudinal line may increase or decrease depending on the UV exposure, whereas the width of the lesion should remain unchanged (Figure 19A, B) [28].

Early and late invasive melanoma of the nail unit

In epidemiological studies, melanoma of the nail unit frequently appeared in patients older than 50 years and, interestingly, was mostly localized at the nail unit of the thumb or the great toe. Approximately 50% of patients with nail melanoma recollect a preceding trauma [3]. The width of the longitudinal pigmentation in melanoma in situ or early invasive melanoma frequently measures more than 5 mm and shows lines of variable thicknesses, spacing, and coloration.
A feature significantly associated with the diagnosis of subungual melanoma is the micro- or macro-Hutchinson sign defined by the visibility of a pigmentation of the periungual cuticula only by dermatoscopy or by naked eye inspection respectively (Figure 20A, B) [29]. Of note, in a number of early invasive subungual melanomas specific criteria may still be absent. In these cases a thorough investigation of the lesional evolution may raise enough suspicion to schedule a matrix biopsy (Figure 21A, B). For other cases, sequential digital dermatoscopy may help to detect dynamic changes in color as well as an increase in width of the whole longitudinal pigmentation over the course of time.

In far advanced invasive melanomas of the nail unit, the diagnosis may be easily made by naked eye examination. The nail unit then often reveals a severe dystrophy of the nail apparatus with ulceration, hemorrhage, or even loss of the overall nail plate. Further criteria for a late invasive melanoma of the nail unit are loss of parallelism, multiple colors and localized invasion of malignant melanoma cells into the adjacent skin (Figure 22A-D, 23A, B). The listed criteria should prompt the clinician to take at least one biopsy of the nail matrix without further delay.

The prognosis of nail matrix melanoma is generally less favorable than for melanoma in other sites due to the frequent delay in diagnosis.

Further indications for dermatoscopy of the nails
Another useful indication for dermatoscopy of nails is the examination of the nail fold capillaries in patients with connective tissue diseases like systemic sclerosis (Figure 24A-B) [30]. In patients suffering from sclerodactyly, the evaluation
of nail fold capillaries should include the degree of dilated capillaries, the extent of nail fold hemorrhage as well as avascular areas. The dermatoscopic documentation of dilated capillaries and/or nail fold hemorrhage is a sensitive and specific strategy for the diagnosis of systemic sclerosis [30].

Summary

Besides the clinical examination, dermoscopy plays an important role in the evaluation of nail disorders. The dermatoscopic criteria for a valid diagnosis have been developed and assessed in numerous clinical trials. In all nail alterations that are suspicious or potentially malignant, a surgical intervention with subsequent histopathological evaluation should be performed. Despite the investment of huge amounts of money for the development of diagnostic medical devices that should help clinicians to diagnose cutaneous melanoma with higher sensitivity and specificity, there is no such device suitable for the application in the case of nail pigmentations. Quite the contrary, numerous manufacturers (e.g., MelaFind®/MelaSciences, Nevisense®/SciBase) explicitly exclude the usage of their devices for the nail unit. Therefore, an extensive training of clinicians in dermatoscopy for lesions in the nail region is essential.

International Dermoscopy Society (IDS)

The International Dermoscopy Society (IDS) offers a valuable panel for further education in this important technique for all colleagues that are interested in dermatoscopy. After registration (free of cost) on the IDS homepage (http://www.dermoscopy-ids.org), a range of tutorials and presentations of cases from all over the world are available. In the discussion forum, the user can upload digital images of uncertain cases and will receive comments from the most prestigious international experts of dermatoscopy within a few days.

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