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Pigmentations of the Nails

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Abstract

Nail pigmentations can exhibit many different colors and shades. Most of them are harmless but cosmetically embarrassing, others are potentially serious and may lead to death if not adequately diagnosed and treated. This short review gives an explanation for a number of nail dyschromias and their etiologies as well as some hints as to their treatment.

Keywords: Nail discoloration; Melanonychia; Ungual melanoma; Microbial pigmentation; Internal diseases

Introduction

Nail pigmentations can exhibit many different colors and shades. Most of them are harmless but cosmetically embarrassing, others are potentially serious and may lead to death if not adequately diagnosed and treated. This short review gives an explanation for a number of nail dyschromias and their etiologies as well as some hints as to their treatment.

Material and Methods

This review is based on 40 years of personal experience with patients having nail changes, the evaluation of their patient charts and more than 50,000 color photographs. The scientific literature was followed back for one century.

Results

Nail discolorations or nail dyschromias are frequently seen in general medicine, in dermatology and particularly in a specialized nail clinic. They may be classified according to their medical relevance or the color displayed, and the latter is the most commonly applied criterion. For most colors, a specific term is known.

Leukonychia

This term (leukos white, onyx nail) designates a white color. Many different forms are known: patchy and diffuse; punctate, striate; longitudinal and transverse, partial and complete, acquired and genetic, idiopathic and induced by a variety of conditions [1]. In addition, apparent and pseudoleukonychia have to be differentiated from true leukonychia.

Punctate leukonychia is particularly frequently seen in young girls when they start to perform their own manicure. It is thought to be of traumatic origin, but this only explains a part of the cases. Punctate und short striate leukonychia is often a sign of a hammer blow when it overlies a subungual hematoma. Crush injuries are usually bigger (Figure1). Transverse leukonychia may be a sign of limited growth retardation, such as after high fever or during chemotherapy cycles. Longitudinal leukonychia is usually the sign of a thread of subungual keratin, such as in subungual filamentous tumor or onychopapilloma. Diffuse leukonychia may be congenital or acquired; the latter is often seen in chronic hepatic disease. When the distal third or half of the nail is normal it is called partial leukonychia. So-called half-and-half nails are a sing of chronic renal failure (Figure 2).

Histologically, leukonychia displays nucleated nail plate cells (onychocytes).

Pallor of the nail bed is seen as apparent leukonychia, pressure on the nail makes is either even more visible or disappear. Pseudoleukonychia is a classical sign of white superficial onychomycosis, which represents a fungal infection of the nail plate surface of toes and is due to *Trichophyton mentagrophytes (interdigitale)* in temperate climates (Figure 3) and to a variety of non-dermatophyte molds in hot climates. Another type of superficial fungal infection is seen in HIV patients and caused by *T rubrum*. Whereas the former exhibits chalk-white patches the latter keeps a nail plate surface shine and resemble a white cloud (Figure 4). A white nail discoloration is further caused by fungal infections that invade the nail plate such as proximal (white) subungual onychomycosis (Figure 5) and endonyx onychomycosis. Finally, virtually all onycholytic parts of a nail and massive subungual keratosis (Figure 6) appear whitish-yellow due to loss of nail plate transparency.

Yellow Nails

Xanthonychia (Greek xanthos yellow) is not rare. It is seen in onychomycoses (Figure 7), psoriasis, onychogryphosis and a variety of onycholysis types overlying oozing processes of the nail bed, such as squamous cell carcinoma or amelanotic melanoma. The most characteristic disease exhibiting xanthonychia is the Yellow Nail Syndrome (YNS). It is characterized by the trias of yellow nails, distal extremity lymphedema and chronic respiratory infection [2]. However, the full trias is not always seen. The most common type of respiratory infections are sino-bronchial syndrome and bronchiectasis [3], but other internal diseases and carcinomas were observed in association with the YNS [4-6]. The nails show a yellow discoloration, the cuticle is lost spontaneously; the nails virtually stop growing and lose their attachment to the nail bed (Figure 8). With time, most of them fall off. The exact mechanism of these nail changes is not known although hypotheses abound, such as anatomical or functional alterations of the lymphatic or vascular microcirculation.

Red Nails

Erythronychia (erythros red) is seen as a spot, a streak or as a diffuse discoloration. Longitudinal erythronychia is a longitudinal streak in the matrix and nail bed. It is most frequently a sign of an

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Figure 1: Traumatic leukonychia after a car door crush injury 3 months ago.



Figure 2: Half-and-half nails of renal insufficiency displaying diffuse leukonychia of the proximal two thirds of the nails.



Figure 3: Chalky white patch on the nail plate surface in white superficial onychomycosis due to *Trichophyton mentagrophytes*.

onychopapilloma, a papillomatous-keratotic lesion of the distal matrix running all along the nail bed to the hyponychium. Other causes are subungual filamentous tumor, Bowen's disease, ungual lichen planus and subungual arteriovenous malformation [7]. As Bowen's disease is an important differential diagnosis a biopsy for histopathological examination is recommended if the diagnosis is not absolutely clear. Multiple red longitudinal lines are a sign of Darier's dyskeratosis follicularis (Figure 9). Red spots in the lunula may be seen in acute psoriasis and alopecia areata. A violaceous area that is extremely sensitive to pressure is a hallmark for a subungual glomus tumor. Angiomas of the nail are surprisingly rare, but they also present as a red area under the nail. However, all inflammations and hyperemic conditions may make the nail look red as the erythema shines through the transparent nail. In port-wine stains, the nail may be diffusely leukonychotic or take on a violaceous hue.

A pink staining of the nails was observed in a patient with hyperhidrosis who had a *Serratia marcescens* colonization [8]. Orangebrown nails were described as a new sign of Kawasaki syndrome [9].

Green Nails

Green nail discoloration is also chloronychia (chloros green). It is a very characteristic sign of *Pseudomonas aeruginosa*, which may both colonize and infect the nail. Most often, the lateral margins from the cuticle to the distal third of the nail are stained dark green (Figure 10). The overlying proximal nail plate shows a mild paronychia and the cuticle is lacking here. Both the upper as well as undersurface of the nail plate (Figure 11) may be colonized with the bacteria that, in histopathology, usually show a bacterial biofilm. Fungal stains often show a co-infection with yeasts and/or dermatophytes. A lake of pus with green color is a sign of a subungual *Pseudomonas aeruginosa* abscess (Figure 12). Also some molds can cause a greenish color, such as *Aspergillus glaucus* (Figure 13) and even *A niger*.

Blue Nails

This color is rarely seen in nails. Even *Aspergillus glaucus* (blue) produces rather a bluish green than a real blue. However, higher concentrations of copper sulfate used as a disinfective agent for swimming pools was observed to cause bluish nails. Blue nails are also a sign of argyria [10,11]. A blue-gray mucocutaneous and nail dyspigmentation was seen as a consequence of ezagabine treatment for epilepsy [12]. In contrast to the familiar term, blue nevi of the matrix and nail bed appear as dark brown spots [13].

Brown and Black Nails

Melanonychia (melanos black) is the potentially most serious type of discoloration as ungual melanoma is the most important differential diagnosis. However, there are many causes for brown to black nails that are conveniently classified into exogenous due to foreign substances or microorganisms and endogenous due to blood or melanin.

Common exogenous causes for brown nails are baths with potassium permanganate; when the concentration is too high manganese dioxide is formed that is laid down on the nail surface as a brown and insoluble substance that can be removed by rubbing the skin with ascorbic acid (vitamin C) solution. Overuse of povidone iodine also stains the nail dark-brown (Figure 14). A dark grey-black stain may be seen with tar contact. It can be removed with petrolatum or other fatty ointments as it is fat-soluble. Heavy smoking may stain the tip of the fingers holding the cigarette brown from the smoke. A greyish dirty stain, particularly on the lateral margins, may be due to

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Figure 4: White superficial onychomycosis of the index finger due to Trichophyton rubrum in an AIDS patient displaying a cloudy appearance.



Figure 5: Proximal subungual white onychomycosis with white bands running parallel to the lunula border; they are thought to reflect systemic spread of dermatophytes.



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Figure 7: Yellow to ocre nail color due to infection with Scopulariopsis brevicaulis.



Figure 8: 48-year-old female patient with full-blown yellow nail syndrome: classical nail changes, distal extremity edema and chronic sinu-bronchial syndrome in addition to Hashimoto's thyroiditis.



Figure 9: Multiple longitudinal red streaks in the nails of a patient with dyskeratosis follicularis of Darier.



Figure 6: Distal subungual onychomycosis causes thick subungual hyperkeratoses that appear yellowish-white.

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Figure 10: Green nail margins with circumscribed paronychia and loss of the cuticle over the green area due to *Pseudomonas aeruginosa*. Histopathologic examination had shown dermatophytes in and *Candida* spp under the nail in addition to the *P aeruginosa* biofilm.



Figure 11: *Pseudomonas aeruginosa* colonization at the undersurface of the onycholytic nail with horseshoe-crab deformity.



Figure 12: Subungual abscess due to Pseudomonas aeruginosa.



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Figure 13: Bluish-green nail discoloration due to Aspergillus glaucus.



Figure 14: Patient with impaired microcirculation who had performed soaks with povidone iodine that stained his nails brown.



Figure 15: Dark grey discoloration due to *Proteus* spp. A slice of nail had been cut from the surface to confirm the diagnosis.

enterobacteria such as *Klebsiella* and *Proteus* spp (Figure 15). They produce sulfur hydrogen that reacts with environment heavy metal trace on the nail surface to metal sulfides.

A variety of fungi produce melanin as a virulence and resistance factor. It is either cytoplasmic or deposited in the fungal cell wall and may be secreted into the environment. In temperate climates *Trichophyton rubrum var nigricans* is the most common cause (Figure 16), but other dermatophytes may also rarely produce pigment. *Alternaria* spp, *Scytalidium dimidiatum*, *Aspergillus* spp (Figure 17), *Candida* spp, a variety of other molds and *pheohyphomycetes* may cause brown nails, either as a diffuse staining or in a striate pattern. *T rubrum var nigricans* usually invades the nail unit from distal and causes a black distal subungual onychomycosis, which shows a narrow wedge with its tip pointing proximally. Histopathologically, a diffuse yellowish-brown stain is seen which is Fontana-negative (Figure 18).

Although the term melanonychia does not necessarily imply it is melanin that stains the nail brown most physicians will automatically think of human melanin. A true melanin production is due to melanocytes. They occur naturally and physiologically in the nail matrix, in a much lower number also in the nail bed. Melanocytes of the distal matrix are more active than those in the proximal (apical) matrix, thus brown streaks more frequently take their origin from the distal matrix and can be localized in the deeper nail plate layers. The melanin produced by matrix melanocytes, which is not degraded by the keratinocytes, is incorporated in the growing nail plate. When present in sufficient amounts it is seen clinically as a light brown to almost jet-black color. Human melanin is granular and hence Fontanapositive; it can easily be distinguished from the diffuse non-granular fungal melanin. Visible melanin may be due to activation of matrix melanocytes without a numerical increase, a lentigo representing a proliferation of melanocytes in basal and suprabasal localization (Figure 18), a nevus showing at least one nest of melanocytes (Figure 19), or a malignant melanoma (Figure 20). Melanocyte lesions in the nail bed do not give pigment to the growing nail plate and thus remain stationary brown to bluish spots.

Approximately two thirds to three quarters of subungual melanomas are pigmented and their earliest sign is then a longitudinal melanonychia (Figure 21): this is why melanonychia is such an important issue in nail pathology. Nail bed melanomas are most often amelanotic (Figure 22). Although nail melanomas make up for only 1.5 - 2.5% of all melanomas in light-skinned individuals the surface of all nails taken together is much less than 1% of the body surface; thus the nail is markedly overrepresented as localization for melanomas.

Melanonychias may be due to local causes, some dermatoses, internal diseases and alimentary conditions as well as tumors.

Melanonychias occurring in dermatologic diseases

Ungual lichen planus is the commonest inflammatory skin condition causing brown streaks in the nail. This is particularly the case in dark-skinned individuals and is comparable to pigmented lichen planus of the skin.

Local causes of longitudinal nail pigmentations

Friction and other chronic repeated traumas are often the reason for nail pigmentation. The first and fifth toes are subject to rubbing in shoes and develop ill-defined brown longitudinal streaks that are mostly located on one side of the nail. Melanonychia was also observed after wart treatment with 5-fluorouracil [14]. Again, this condition is much more frequent in deeply pigmented people. Histologically, an increased pigmentation without numerical melanocyte numbers is seen.

Internal diseases

Many general disorders may increase skin and nail pigmentation, such as Nelson's syndrome, adrenal insufficiency [15], pituitary adenoma [16], vitamin B_{12} deficiency, very many drugs like zidovudine, antimalarials, chlorpromazine, tinzarapin [17], a variety of internal tumors and cytostatic treatments (cyclophosphamide, doxorubicine, docetaxel) [18,19] the latter sometimes causing short-lasting melanocyte activation with transverse dark bands in the nails (Figure 23).

Tumors

Longitudinal brown bands were also seen due to non-melanocytic tumors, such as onychopapilloma [20], onychomatricoma [21,22], subungual keratotic hyperplasia [23,24], onychocytic matricoma [25], Bowen's disease [26,27], squamous cell carcinoma [28], even basal cell carcinoma [29]. Lentigines, nevi and melanomas are, however, the most frequent cause.

The Melanonychia Dilemma

As briefly mentioned above, brown pigmentation of the nail is the most common sign of ungual melanoma. However, one quarter to one third of nail melanomas are amelanotic. The rate of misdiagnoses is very high with resulting delay in treatment and poor prognosis. A few signs are suggestive for a malignant process [30]. The melanonychia started developing in adult age.

- It is monodigital, particularly on thumb, index, middle finger and big toe.
- The band widen and has a diameter greater than 5 mm.
- Close inspection reveals periungual pigmentation, the Hutchinson sign.
- There is a nail dystrophy, even when barely noticeable.
- A bleeding tumor is already a sign of invasion.

As only a certain percentage of melanonychias is malignant it is of paramount importance to make the correct diagnosis to avoid underdiagnosis with the potential of missing the correct time for adequate treatment and not to overdiagnose a benign lesion and perform a potentially mutilating procedure.

Melanonychias are usually benign when

- they are observed in darkly pigmented individuals,
- occur in children,
- are multidigital,
- develop during or shortly after a cytostatic therapy.

However, even three nail melanomas were observed in one patient and also in children (Figure 24) [31,32].

When one faces a longitudinal melanonychia, the nature of the pigment has to be determined first. Human melanin can be demonstrated as fine granules with the Fontana-Masson argentaffin reaction. Fungal melanin is diffuse and not stained with Fontana. Blood is positive with the pseudocatalase reaction, but negative with Prussian blue stain. Exogenous pigments can be scraped off, lipidsoluble substances like tar disappear during the histologic processing.



Figure 16: Black spikes in a black onychomycosis due to T rubrum var nigricans.





Figure 17b: Histologic section of a case of black onychomycosis showing diffuse brown staining of the nail plate substance in addition to numerous PAS-positive hyphae.



Figure 18: Longitudinal melanonychia in a 5-year-old child due to a matrix lentigo.



Figure 19: Longitudinal melanonychia in a 20-year-old man due to a matrix nevus.



Figure 20: *In situ* melanoma with extensive periungual pigment spread (Hutchinson sign).

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Figure 21: Early invasive subungual melanoma. Note the barely visible notch in the nail's free margin.



Figure 22: Amelanotic invasive and protuberant melanoma of the lateral nail bed.



Figure 23: Melanonychia due to cyclophosphamide treatment in a patient with mammary carcinoma.



Figure 24: Dermatoscopy of this melanonychia in an 11-year-old girl shows irregular banding and was diagnosed histologically as melanoma *in situ*.





Figure 25: 34-year-old female patient with a regular longitudinal melanonychia.

- α.
- β.
- Normal clinical photograph. "Dry" dermatoscopy (without an immersion medium). "Wet" dermatoscopy using ultrasound gel makes more χ. details visible.



Figure 26: Narrow light brown longitudinal melanonychia in a 72-year-old woman indicating an early melanoma.



Figure 27: Amelanotic melanoma that had been treated as granulation tissue with silver nitrate, which stained part of the lesion black and initiated her referral to our department.



Figure 28: Ulcerated amelanotic melanoma of the lateral nail bed and phalanx that had been treated as an ingrown nail for more than 6 years.



Figure 29: Far advanced melanoma, mainly amelanotic, but with a margin of brown pigmentation; it had been misdiagnosed as an agioma.



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Figure 30: Far advanced metastasizing melanoma mistreated as onychomycosis for many years.

Silver nitrate used to cauterize granulation tissue causes round black dots in the superficial nail plate.

Whereas melanin can be identified histologically it gives no information as to the dignity of the lesion; however, sometimes some single pycnotic melanocytes can be seen in the nail plate, which is generally accepted as a sign of melanoma as it represents pagetoid spread of melanoma cells.

Analogous to the ABCD rule for cutaneous melanomas, a diagnostic aid, the ABCDEF rule, has been developed for nail melanomas [33].

A – age and race: most nail melanomas occur in persons between 40 and 70 years of age. African Americans, native Americans, and Asians have a higher percentage of ungual melanomas.

B – **b**rown to black longitudinal band in the nail; breadth >3 mm; border irregular or blurred.

C – change: rapid increase in width and growth rate. Nail dystrophy does not improve despite "adequate treatment."

D – **d**igit: thumb > big toe > index finger; single digit involvement, two or more nails very rarely affected.

E – **e**xtension of pigmentation: Hutchinson's sign.

F – family or personal history of melanoma or so-called dysplastic nevi.

These criteria are helpful for pigmented but not for amelanotic melanomas, and their value in children remains to be elucidated [34].

Dermatoscopy is often an aid to the diagnosis of pigmented (and non-pigmented) lesions of the skin and has also been applied to nail pigmentations (Figure 25). Although it is able to give additional information, particularly as to the nature of the pigment and micro-Hutchinson sign, it cannot replace histopathology [35]. It is useful as series dermatoscopy to evaluate the development [36]. An automated evaluation system for melanonychias was developed to overcome the subjectivity in measuring and interpreting the results [37]. It is assumed to be able to reliably distinguishing between benign and malignant melanonychias. Intraoperative matrix dermatoscopy increases the diagnostic accuracy [38,39]. Perioperative reflectance confocal laser scanning microscopy was claimed to allow an immediate *ex vivo* diagnosis to be made with the surgical excision specimen [40].

Pigmentary Disorders

Functional melanonychia versus matrix lentigo and nevus

Banded longitudinal brown nail pigmentation is not rare; it may be called physiological in deeply pigmented races and is quite frequent in Africans and Asians. However, repeated microtrauma may also elicit activation of matrix melanocytes with consequent melanin overproduction leading to longitudinal melanonychia. Many drugs also cause increased melanin production. All these conditions do not demonstrate a numerical increase in the number of melanocytes. These brown bands are therefore called functional melanonychia.

In contrast, lentigines and nevi are defined by an increase in the number of melanocytes in the matrix. In lentigines, there is a proliferation of melanocytes in the basal and suprabasal matrix epithelium whereas in nevi, the melanocytes are also arranged in nests. These nests may be located both in the lower matrix epithelium and the dermis although the latter is comparatively rare. Lentigines and nevi in the matrix produce melanin, the excess of which is deposited in the nail plate and continuously transported distally thus giving rise to the longitudinal band. From time to time, nevus cell nests may migrate upward and become included into the nail plate; this is well seen in dermatoscopy and may even be a sign of nevus regression in children [41].

In general, it is difficult to make a clear-cut reliable distinction between a benign and malignant melanonychia and only histopathology is accepted as being the diagnostic gold standard. Although most authors agree with this statement they usually try to find measures to avoid a biopsy, probably because they lack experience with nail surgery and out of fear to produce a post-biopsy nail dystrophy [42-44].

We have developed a technique to superficially, but completely remove melanocyte lesions in the matrix and nail bed that virtually leaves no postoperative nail dystrophy [45-49]. A proximal digital block or transthecal anesthesia is applied, preferably using a longacting local anesthetic such as ropivacaine. A tourniquet is then applied. The Proximal Nail Fold (PNF) is pushed back to allow the beginning of the lesion to be identified. If this is not enough, the PNF is incised on both sides and detached from the underlying nail plate. This is gently separated from the underlying matrix with a nail elevator using the proximal approach. The plate is then cut transversely from one side to just 3 mm beyond the border of the brown streak and this nail flap is elevated like a trap door exposing the matrix melanocyte focus. A shallow incision is carried around the lesion with an adequate safety margin. The #15 scalpel blade is then laid flat and with some gentle pressure on the matrix, horizontal back-and-forth movements are made to tangentially remove the lesion with a tissue slice being 0.7 to 1 mm thick. The specimen is transferred onto wet gauze and then spread on filter paper to be immersed into the fixative. A drawing may have been made on the filter paper to indicate the exact localization of the melanocyte spot in the matrix. The raised portion of the nail plate is laid back and fixed with a stitch and then the PNF is stitched back into position. The tourniquet is released. A thick padded dressing is applied and changed the next day. Postoperative pain is minimal and does not start before 16 to 24 h after surgery. Healing takes place within a few days. The stitches are removed after 12 to 14 days. The detached nail plate portion can later be fixed with adhesive tape or acrylic glue, or may be cut. In case the histologic examination revealed a malignant lesion the entire nail organ with a minimum of 6 mm around the anatomic borders of the nail is excised down to the bone and dorsal aponeurosis. The defect may be left for second intention healing or be repaired with a full-thickness skin graft or other techniques.

The thin tissue specimen allows the complete histologic examination

of the lesion [50,51]. Although recurrence of pigmentation may be seen when the safety margin is too small it is a very safe method to make a correct diagnosis [52]. In our opinion, there is no excuse for watching a melanonychia becoming a metastasizing ungual melanoma.

Nail Melanoma

Virtually all publications claim that the diagnosis of nail melanomas is difficult and that this is the reason for delay in diagnosis and particularly for poor prognosis. Whereas the latter is true, the diagnosis is not difficult, at least not for pigmented melanomas. Awareness of the possibility of nail melanomas is the critical point. Most nail melanomas are pigmented and arise in the matrix. Those in the nail bed are often, but not always, amelanotic and even when pigmented they do not produce a longitudinal melanonychia, but sometimes a Hutchinson sign. Nail melanomas have their peak incidence between 50 and 60 years, but the age range is wide from childhood to over 90 years of age. It is our policy to biopsy all longitudinal melanonychias in adults - with the exception of functional melanonychia when this is obvious - and all brown bands in children and adolescents if the parents or patients want it. The proportion of thick invasive nail melanomas in our practice has thus decreased dramatically. A recently appearing melanotic band in a fair-skinned adult is always suspicious, and a jet-black or otherwise differing band in the nail of a person with racial nail pigmentation is also suspicious [53]. Early melanoma of the matrix can be very difficult to diagnose histopathologically [54]. It is known that small cutaneous melanomas may lack the histopathologic criteria to make this diagnosis [55] It is our experience that this also happens with nail melanomas (Figure 26). Although the lesion may histomorphologically appear relatively bland it is biologically malignant.

The etiology of nail melanomas is unclear. Trauma has been implicated in its genesis but the time-development relation is often not convincing. Ultraviolet light is most probably not the cause as the nail plate is a very effective shield and the nail fold covers most of the matrix [56]. However, a trauma may be the reason to consult a dermatologist and thus lead to the diagnosis of nail melanoma [57]. This also explains why melanomas diagnosed after trauma were thicker.

Nail Melanoma Treatment

The treatment of melanomas is surgical. In situ and early invasive melanomas can be treated with wide local excision as was already shown more than 35 years ago [58]. Many publications have proven our conservative approach [59-62]. A large comparative study has shown that amputation does not benefit the patients [63].

Discussion

Nail discolorations are varied in color and importance. Whereas some of the many different types of leukonychias as well as a variety of other nail dyschromias may give a hint at a particular underlying pathology the really serious condition is brown to black as it may represent nail melanoma. However, melanomas of the nail unit may also be amelanotic (Figure 27); an "ingrown nail" in an adult beyond the age of 30 (Figure 28), a "wart" in an adult, an acquired "angioma" (Figure 29) and even a "long-standing onychomycosis" (Figure 30) may be a melanoma. Onycholysis with oozing is a particularly serious warning sign as it is characteristic for both subungual squamous cell carcinoma as well as nail bed melanoma.

It is continuously stated that ungual melanomas have a poor prognosis because they are difficult to diagnose. This statement is only partially correct as the diagnosis, at least for pigmented melanoma, does not really pose a diagnostic challenge - as long as you think of the possibility of melanoma. This is the weak point! Series of ungual melanomas with 100 cases and more have shown tumor thicknesses of 4 mm and more [64-66]. This is evidence of tremendous neglect, both from the side of the patients as well as their physicians.

Treatment of nail melanomas has long been amputation of the digit. The prognosis was not better [57] Comparison of amputation levels metacarpo/metatarsal-phalangeal, proximal or distal interphalangeal did not show different survival rates [67]. Local excision has proven to be superior to amputation [68]. It is the time of treatment that decides the prognosis. It is probably not incorrect to say that amputation did hardly ever save a life since when it is too late for wide local excision amputation is also no longer able to cure the patient.

References

- Kim SW, Kim MS, Han TY, Lee JH, Son SJ (2014) Idiopathic acquired true leukonychia totalis and partialis. Ann Dermatol 26: 262-263.
- 2. Dhillon SS (2012) Yellow nail syndrome. Am J Respir Crit Care Med 186: e10.
- Modrzewska K1, FijoÅ,ek J, Ptak J, Wiatr E (2012) [Yellow nail syndrome in a patient with membranous glomerulonephritis]. Pneumonol Alergol Pol 80: 158-162.
- 4. Tidder J, Pang CL (2012) A staged management of prolonged chylothorax in a patient with yellow nail syndrome. BMJ Case Rep 2012.
- Letheulle J, Deslée G, Guy T, Lebargy F, Jego P, et al. (2012) [The yellow nail syndrome: a series of five cases]. Rev Mal Respir 29: 419-425.
- Noël-Savina E, Paleiron N, Leroyer C, Descourt R (2012) [Discovery of a yellow nail syndrome with major hypothyroidism]. Rev Pneumol Clin 68: 315-317.
- Rutnin S, Nguyen JV, Miller CJ, Dehoratius D, Rubin AI (2012) Pregnancyassociated acquired arteriovenous malformation of the nail unit: a novel cause of localized erythronychia. J Cutan Pathol 39: 1030-1034.
- Harada K, Morohoshi T, Ikeda T, Shimada S (2012) A patient with pseudochromhidrosis presenting with pink nails. J Am Acad Dermatol 67: e74-75.
- Pal P, Giri PP (2013) Orange-brown chromonychia, a novel finding in Kawasaki disease. Rheumatol Int 33: 1207-1209.
- Kim Y, Suh HS, Cha HJ, Kim SH, Jeong KS, et al. (2009) A case of generalized argyria after ingestion of colloidal silver solution. Am J Ind Med 52: 246-250.
- 11. Raychaudhuri SP, Raychaudhuri S (2014) The blue nails of argyria. Int J Dermatol 53: e400-401.
- Garin Shkolnik T, Feuerman H2, Didkovsky E3, Kaplan I4, Bergman R5, et al. (2014) Blue-gray mucocutaneous discoloration: a new adverse effect of ezogabine. JAMA Dermatol 150: 984-989.
- Lee EJ, Shin MK, Lee MH (2012) A subungual blue naevus showing expansile growth. Acta Derm Venereol 92: 162-163.
- 14. De Anda MC, Domínguez JG (2013) Melanonychia induced by topical treatment of periungual warts with 5-fluorouracil. Dermatol Online J 19: 10.
- Prat C, Viñas M, Marcoval J, Jucglà A (2008) Longitudinal melanonychia as the first sign of Addison's disease. J Am Acad Dermatol 58: 522-524.
- 16. Schepis C, Siragusa M, Palazzo R, Piraccini BM (2013) Multiple melanonychia as a sign of pituitary adenoma. Clin Exp Dermatol 38: 689-690.
- Takci Z, Ozoguz P (2012) Nail discoloration due to tinzaparin sodium. Cutan Ocul Toxicol 31: 332-334.
- Steele JC, Triantafyllou A, Rajlawat BP, Field EA (2012) Oral mucosal hyperpigmentation and horizontal melanonychia caused by imatinib. Clin Exp Dermatol 37: 432-433.
- 19. Poppe LM, Bröcker EB, Trautmann A (2013) The one-nail brown band: macroand micro-morphology. Acta Derm Venereol 93: 479-480.
- Miteva M, Fanti PA, Romanelli P, Zaiac M, Tosti A (2012) Onychopapilloma presenting as longitudinal melanonychia. J Am Acad Dermatol 66: e242-243.
- 21. Wang L, Gao T, Wang G (2014) Nail bed onychomatricoma. J Cutan Pathol
- 22. Wynes J, Wanat KA, Huen A, Mlodzienski AJ, Rubin AI (2014) Pigmented onychomatricoma: A rare pigmented nail unit tumor presenting as longitudinal

melanonychia that has potential for misdiagnosis as melanoma. J Foot Ankle Surg.

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- Baran R, Perrin C (1999) Linear melanonychia due to subungual keratosis of the nail bed: a report of two cases. Br J Dermatol 140: 730-733.
- Okamoto O, Ishikawa K, Kai Y, Yokoyama S, Fujiwara S (2012) Longitudinal melanonychia caused by unusual subungual keratosis. J Dermatol 39: 930-931.
- Perrin C, Cannata GE, Bossard C, Grill JM, Ambrossetti D (2012) Onychocytic matricoma presenting as pachymelanonychia longitudinal. A new entity (report of five cases). Am J Dermatopathol 34: 54-59
- Sass U, André J, Stene JJ, Noel JC (1998) Longitudinal melanonychia revealing an intraepidermal carcinoma of the nail apparatus: detection of integrated HPV-16 DNA. J Am Acad Dermatol 39: 490-493.
- Saito T, Uchi H, Moroi Y, Kiryu H, Furue M (2012) Subungual Bowen disease revealed by longitudinal melanonychia. J Am Acad Dermatol 67: e240-241.
- Fernandes Massa A, Debarbieux S, Depaepe L, Dalle S, Balme B, et al. (2013) Pigmented squamous cell carcinoma of the nail bed presenting as a melanonychia striata: diagnosis by perioperative reflectance confocal microscopy. Br J Dermatol 169: 198-199.
- Rudolph RI (1987) Subungual basal cell carcinoma presenting as longitudinal melanonychia. J Am Acad Dermatol 16: 229-233.
- Haneke E, Baran R (2001) Longitudinal melanonychia. Dermatol Surg 27: 580-584.
- Iorizzo M, Tosti A, Di Chiacchio N, Hirata SH, Misciali C, et al. (2008) Nail melanoma in children: differential diagnosis and management. Dermatol Surg 34: 974-978.
- Tosti A, Piraccini BM, Cagalli A, Haneke E (2012) In situ melanoma of the nail unit in children: report of two cases in fair-skinned Caucasian children. Pediatr Dermatol 29: 79-83.
- Levit EK, Kagen MH, Scher RK, Grossman M, Altman E (2000) The ABC rule for clinical detection of subungual melanoma. J Am Acad Dermatol 42: 269-274.
- 34. Di Chiacchio ND, Farias DC, Piraccini BM, Hirata SH, Richert B, et al. (2013) Consensus on melanonychia nail plate dermoscopy. An Bras Dermatol 88: 309-313.
- Adigun CG, Scher RK (2012) Longitudinal melanonychia: when to biopsy and is dermoscopy helpful? Dermatol Ther 25: 491-497.
- Sawada M, Yokota K, Matsumoto T, Shibata S, Yasue S, et al. (2014) Proposed classification of longitudinal melanonychia based on clinical and dermoscopic criteria. Int J Dermatol 53: 581-585.
- 37. Koga H, Yoshikawa S, Sekiguchi A, Fujii J, Saida T, et al. (2014) Automated evaluation system of dermoscopic images of longitudinal melanonychia: Proposition of a discrimination index for detecting early nail apparatus melanoma. J Dermatol.
- Hirata SH, Yamada S, Almeida FA, Enokihara MY, Rosa IP, et al. (2006) Dermoscopic examination of the nail bed and matrix. Int J Dermatol 45: 28-30.
- Hirata SH, Yamada S, Enokihara MY, Di Chiacchio N, de Almeida FA, et al. (2011) Patterns of nail matrix and bed of longitudinal melanonychia by intraoperative dermatoscopy. J Am Acad Dermatol 65: 297-303.
- Debarbieux S, Hospod V, Depaepe L, Balme B, Poulalhon N, et al. (2012) Perioperative confocal microscopy of the nail matrix in the management of in situ or minimally invasive subungual melanomas. Br J Dermatol 167: 828-836.
- Murata Y, Kumano K (2012) Dots and lines: a dermoscopic sign of regression of longitudinal melanonychia in children. Cutis 90: 293-296, 301.
- 42. Ronger S, Touzet S, Ligeron C, Balme B, Viallard AM, et al. (2002) Dermoscopic examination of nail pigmentation. Arch Dermatol 138: 1327-1333.
- Thomas L, Dalle S (2007) Dermoscopy provides useful information for the management of melanonychia striata. Dermatol Ther 20: 3-10.
- 44. Lazaridou E, Giannopoulou C, Fotiadou C, Demiri E, Ioannides D (2013) Congenital nevus of the nail apparatus--diagnostic approach of a case through dermoscopy. Pediatr Dermatol 30: e293-294.
- 45. Haneke E (1999) Operative Therapie akraler und subungualer Melanome. In: Operative und onkologische Dermatologie. Fortschritte der operativen und onkologischen Dermatologie. Springer, Berlin. 15: 210–214.

- Haneke E, Lawry M (2005) Nail surgery. Surgery of the skin. Elsevier, Philadelphia, PA, USA: 719–742.
- Haneke E (2005) Cirugía ungueal. Dermatología práctica Ibero-Latinoamericana. Atlas, enfermedades sistémicas asociadas y terapéutica. DF: Nieto Editores, México. 1643–1652.
- 48. Haneke E (2011) Matrix surgery: tangential excision. In: Richert B, Di Chiacchio N, Haneke E, eds. Nail surgery. Informa Health Care, London and New York : 129–131
- 49. Haneke E (2011) Advanced nail surgery. J Cutan Aesthet Surg 4: 167-175.
- 50. Di Chiacchio N, Loureiro WR, Michalany NS, Kezam Gabriel FV (2012) Tangential Biopsy Thickness versus Lesion Depth in Longitudinal Melanonychia: A Pilot Study. Dermatol Res Pract 2012: 353864.
- Di Chiacchio N, Loureiro WR, Michalany NS, Haneke E (2013) tangential excision for the diagnosis and/or treatment of longitudinal melanonychias. Dermatol Rev Mex 57: 289-293.
- 52. Richert B, Theunis A, Norrenberg S, André J (2013) Tangential excision of pigmented nail matrix lesions responsible for longitudinal melanonychia: evaluation of the technique on a series of 30 patients. J Am Acad Dermatol 69: 96-104.
- Kopf AW, Waldo E (1980) Melanonychia striata. Australas J Dermatol 21: 59-70.
- Weedon D, Van Deurse M, Rosendahl C (2012) "Occult" melanocytes in nail matrix melanoma. Am J Dermatopathol 34: 855.
- 55. Rosendahl C, Cameron A, Bulinska A, Harding-Smith D, Weedon D (2012) Embryology of a melanoma? A case report with speculation based on dermatoscopic and histologic evidence. Dermatol Pract Concept 2: 204a08.
- 56. Rosendahl C, Cameron A, Bulinska A, Harding-Smith D, Weedon D (2012) Embryology of a melanoma? A case report with speculation based on dermatoscopic and histologic evidence. Dermatol Pract Concept 2: 204a08.

- 57. Fanti PA, Dika E, Misciali C, Vaccari S, Barisani A, et al. (2013) Nail apparatus melanoma: is trauma a coincidence? Is this peculiar tumor a real acral melanoma? Cutan Ocul Toxicol 32: 150-153.
- Haneke E (2012) Ungual melanoma controversies in diagnosis and treatment. Dermatol Ther 25: 510-524.
- 59. Haneke E, Binder D (1978) [Subungual melanoma with linear nail pigmentation]. Hautarzt 29: 389-391.
- Duarte AF, Correia O, Barros AM, Azevedo R, Haneke E (2010) Nail matrix melanoma in situ: conservative surgical management. Dermatology 220: 173-175.
- Chow WT, Bhat W, Magdub S, Orlando A (2013) In situ subungual melanoma: digit salvaging clearance. J Plast Reconstr Aesthet Surg 66: 274-276.
- Mannava KA, Mannava S, Koman LA, Robinson-Bostom L, Jellinek N (2013) Longitudinal melanonychia: detection and management of nail melanoma. Hand Surg 18: 133-139.
- Neczyporenko F, André J, Torosian K, Theunis A, Richert B (2014) Management of in situ melanoma of the nail apparatus with functional surgery: report of 11 cases and review of the literature. J Eur Acad Dermatol Venereol 28: 550-557.
- Moehrle M, Metzger S, Schippert W, Garbe C, Rassner G, et al. (2003) "Functional" surgery in subungual melanoma. Dermatol Surg 29: 366-374.
- 65. Blessing K, Kernohan NM, Park KG (1991) Subungual malignant melanoma: clinicopathological features of 100 cases. Histopathology 19: 425-429.
- Thai KE, Young R, Sinclair RD (2001) Nail apparatus melanoma. Australas J Dermatol 42: 71-81.
- 67. Tan KB, Moncrieff M, Thompson JF (2007) Subungual melanoma: a study of 124 cases highlighting features of early lesions, potential pitfalls in diagnosis, and guidelines for histologic reporting. Am J Surg Pathol 31: 1902-1912.
- Slingluff CL Jr, Vollmer R, Seigler HF (1990) Acral melanoma: a review of 185 patients with identification of prognostic variables. J Surg Oncol 45: 91-98.

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