Dermatology Practical & Conceptual

Seven Plus One Steps to Assess Pigmented Nail Bands (Melanonychia Striata Longitudinalis)

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Citation: Lallas A, Korecka K, Apalla Z, et al. Seven Plus One Steps To Assess Pigmented Nail Bands (Melanonychia Striata Longitudinalis). *Dermatol Pract Concept*. 2023;13(4):e2023204. DOI: https://doi.org/10.5826/dpc.1304a204

Accepted: February 21, 2023; **Published:** October 2023

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Funding: None.

Competing Interests: None.

Authorship: All authors have contributed significantly to this publication.

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ABSTRACT

Melanonychia striata longitudinalis might involve one or more fingers and/or toes and might result from several different causes, including benign and malignant tumors, trauma, infections, and activation of melanocytes that might be reactive or related to the pigmentary trait, drugs and some rare syndromes. This broad differential diagnosis renders the clinical assessment of melanonychia striata particularly challenging. Nail matrix melanoma is relatively rare, occurs almost always in adults involves more frequently the first toe or thumb. The most common nail unit cancer, squamous cell carcinoma / Bowen disease (SCC) of the nail matrix is seldom pigmented. Histopathologic examination remains the gold standard for melanoma and SCC diagnosis, but excisional or partial biopsies from the nail matrix require training and is not routinely performed by the majority of clinicians. Furthermore, the histopathologic evaluation of melanocytic lesions of the nail matrix is particularly challenging, since early melanoma has only bland histopathologic alterations. Dermatoscopy of the nail plate and its free edge significantly improves the clinical diagnosis, since specific patterns have been associated to each one of the causes of melanonychia. Based on knowledge generated and published in the last decades, we propose herein a stepwise diagnostic approach for melanonychia striata longitudinalis: 1) Hemorrhage first 2) Age matters 3) Number of nails matters 4) Free edge matters 5) Brown or gray? 6) Size matters 7) Regular or irregular and, finally, “follow back”.

Introduction

Melanonychia striata longitudinalis is a term of Greek-Latin origin still used to describe the presence of a proximal to-distal linear pigmentation of the nail plate [1-3]. A pigmented nail band might have variable width, might involve one or more fingers and/or toes and might result from several different causes [1,3,4]. The list of disorders that may cause nail pigmentation includes benign and malignant tumors, trauma, infections, and activation of melanocytes that might be reactive or related to the pigmentary trait, drugs and some rare syndromes [5]. This broad differential diagnosis renders the clinical assessment of melanonychia striata particularly challenging.

Among the various possible causes of melanonychia striata, melanoma is definitely the most important to be clinically recognized at the earliest possible stage. Nail melanoma is relatively rare, representing 0.7%-3.5 % of all melanomas [6]. Usually, it is diagnosed during adulthood and more frequently involves the first toe or thumb. Nail melanoma almost always develops in the nail matrix, but, since a large proportion of matrix is hidden in the proximal nail fold, what is macroscopically visible is a pigmented band on the nail plate, originating from the proximal nail fold and extending linearly towards the periphery until the distal ending of the nail plate. The pathogenesis of nail melanoma is poorly understood, unlike other melanoma types the role of ultraviolet exposure is probably minimal, it belongs to the lentiginous pathology subtype of melanomas (Acral Lentiginous melanoma [ALM]) characterized by an initial slow growth profile and a little tumor load at early stage. Its evolution towards a more aggressive and visible tumor with an ulcerated and nodular, often amelanotic, component occurs after months of years of apparently indolent melanonychia striata. Prognosis, correlated with Breslow index just like every melanoma subtype, is then clearly impaired underlining the importance of an earlier diagnosis at the melanonychia striata stage. Its genotypic profile very rarely shows BRAF or NRAS mutations yet CKIT mutations appears to be more unusual than initially thought [7,8].

During the last 20 years, dermatoscopy acquired an invaluable role in the diagnosis of pigmented and non-pigmented skin tumors, improving the detection of melanoma and other skin cancers and the recognition of benign tumors as well [9]. Indeed, robust evidence confirms that dermatoscopy increases both the sensitivity and specificity for melanoma diagnosis [10]. However, biopsy and histopathologic examination remain the gold standard procedure for lesions that cannot be safely diagnosed on clinical and dermatoscopic examination. A partial or excisional biopsy is usually an easy to perform procedure, without significant requirements in time and costs and with minimal morbidity or discomfort for the patients. Therefore, there is no significant barrier for clinicians to excise equivocal lesions located on the trunk or extremities or biopsy doubtful lesions on anatomically sensitive areas such as the face.

In contrast, an excisional or partial biopsy form the nail matrix is a much more demanding procedure that requires training and is not routinely performed by the majority of clinicians [11]. It is considered as a complex, painful procedure with an associated risk of a permanent damage to the nail plate, although the latter is not necessarily true. Furthermore, the histopathologic evaluation of melanocytic lesions of the nail matrix is particularly challenging, since early melanoma has only bland histopathologic alterations [12,13].

Taken all the above into consideration, an accurate clinical evaluation of melanonychia striata is particularly relevant and valuable in the routine practice. Based on knowledge generated and published in the last decades, we propose herein a seven-step diagnostic approach for melanonychia striata longitudinalis aiming to provide succinct, comprehensive and clinically useful recommendations.

Step 1. Hemorrhage First

In individuals of white skin, subungual hemorrhage is by far the most common cause of nail plate pigmentation. Therefore, the "pre-test" probability of blood being responsible for nail plate pigmentation is definitely high. Usually, the recognition of a subungual hemorrhage is straight forward on clinical and dermatoscopic examination. It is typified by an initially red-to purple color, sharply demarcated borders, peripheral blood spots and/or linear distal projections (filamentous lines). Over time the color often turns brown yet the silhouette with a sharp proximal border and distal projections does not change. (Figures 1 and 2) [14-16]. Moreover, hemorrhages often do not arise from the proximal nail fold, which helps to exclude melanocytic tumors that always develop on the nail matrix and, therefore, result to nail bands originating from the proximal nail fold (Figure 1).

However, it has to be underlined that the presence of hemorrhage does not exclude the co-existence of a malignant tumor, such as melanoma or squamous cell carcinoma, that might destroy the nail bed and cause bleeding (Figures 3 and 4) [17-19]. For this reason, the diagnosis of a subungual hemorrhage should prompt clinicians to perform a photographic documentation and follow up at a 3-6 months interval in order to monitor the migration, at approximately half the speed of the nail growth one, of the blood towards the distal end and the restitution of the nail plate.

Considering that hemorrhage is the most frequent cause, the assessment of most nail pigmentations will end at this first step. If, however, a hemorrhage cannot be diagnosed with confidence on clinical and dermatoscopic examination, the evaluation should proceed to step 2.

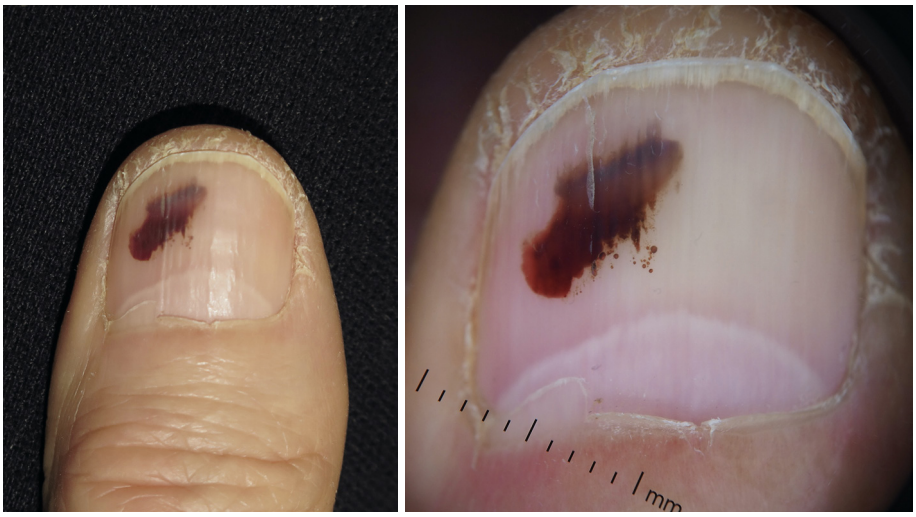

Figure 1. A subungual hemorrhage not arising from the proximal nail fold. Dermatoscopically is it typified by red color, sharp demarcation and satellite blood spots.

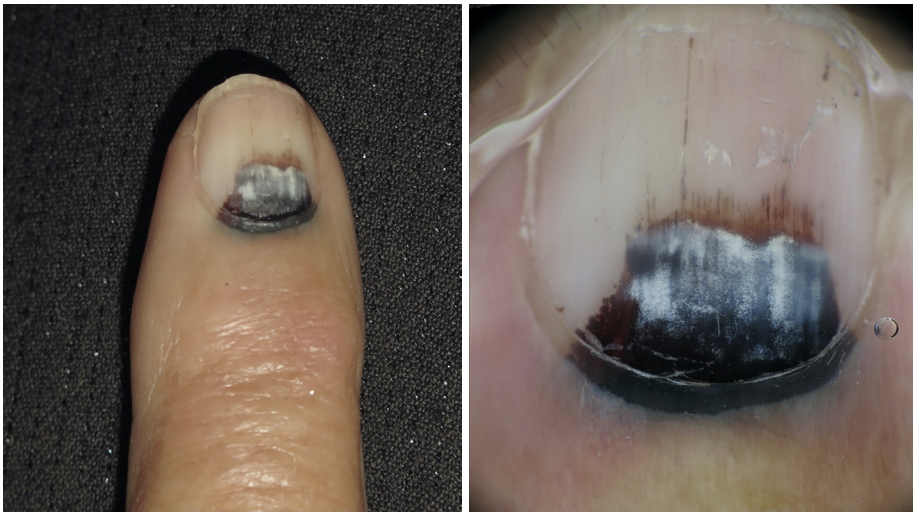

Figure 2. A subungual hemorrhage arising from the proximal nail fold. Dermatoscopy reveals red, purple and black colors and the characteristic linear hemorrhages at the distal part.

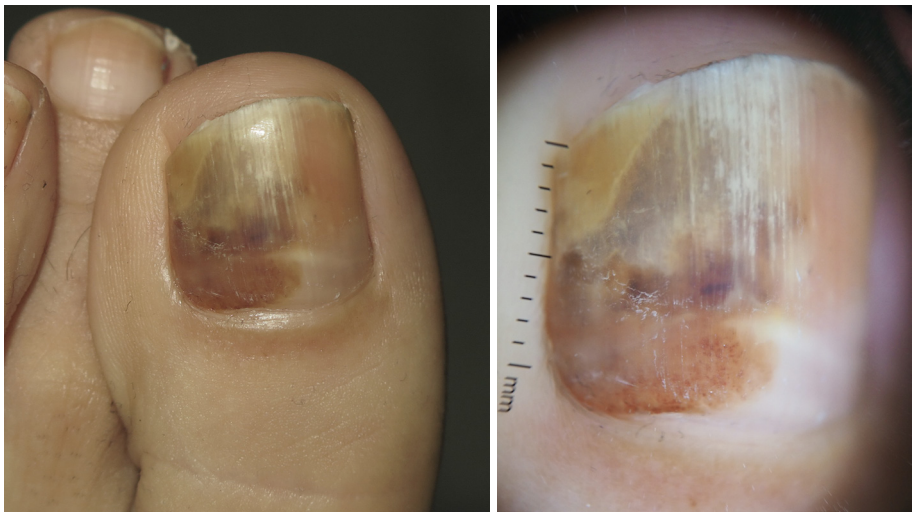

Figure 3. A subungual squamous cell carcinoma complicated with hemorrhage.

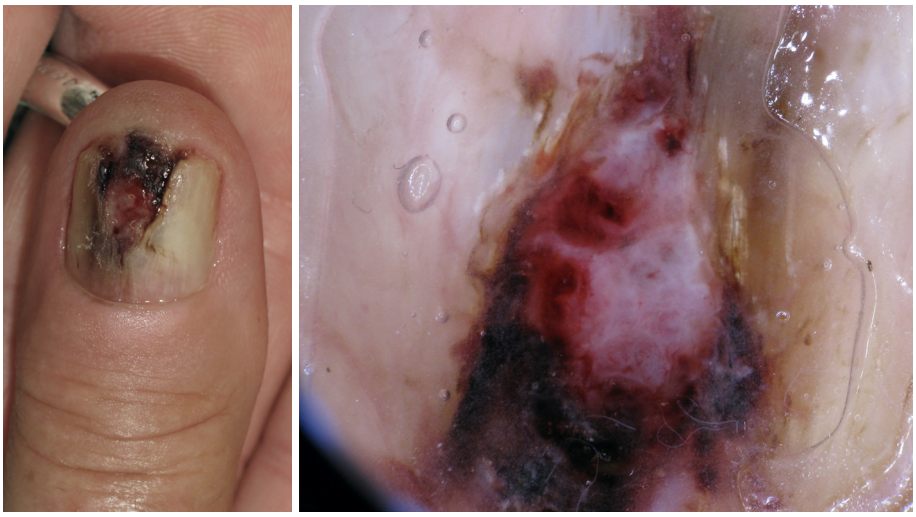

Figure 4. An advanced subungual melanoma that destroyed a significant part of the nail plate and caused hemorrhage.

Step 2. Age Matters

Nail melanoma in childhood is exceedingly rare. Overall, 21 cases have been reported in the literature, of which only two in white individuals [20-22]. In most of these case reports, the histopathologic diagnosis was equivocal and all but 2 lesions were intraepidermal (in situ). There are only 2 reported cases with an unequivocal diagnosis of invasive melanoma developing in a Chinese and a Japanese child, respectively. In large reported series of nail melanoma from referral centers, no patient was younger than 30 years old [19,23]. A study by Blessing et al on 100 cases of subungual melanoma revealed no malignancy in the age group below 30 years old. In another study by Phan et al with 126 cases of acral and nail melanoma, patients age ranged from 28 to 91 years [19,23]. In published series of longitudinal melanonychia in children, no melanoma case was reported [24]. The latter epidemiologic information becomes even more relevant in the light of evidence suggesting that congenital subungual nevi might be particularly worrisome in terms of their clinical and dermatoscopic morphology and also in terms of their growth rate. Nail matrix nevi may be present at birth (congenital), but they can also appear during the first years of life (congenital type) [25]. A recently published multicentric cohort study by the International Dermoscopy Society found that more than half of congenital and congenital-type nail matrix nevi displayed an irregular pattern of longitudinal microlines, reminiscent of subungual melanoma [26].

Therefore, it appears that any pigmented nail band in children is most likely benign, usually caused by a congenital nail matrix nevus, even if the lesion is large, dermatoscopically irregular or extends to the periungual skin (Figures 5 and 6) [22]. While many of these lesions may cause anxiety in the children parents or guardians, evidence suggests they are most likely benign and may only require a regular follow-up.

Step 3. Number of Nails Matters

Nail matrix cancer usually involves only one finger or toe. Thus, longitudinal melanonychia affecting multiple nails is rather suggestive of a systemic factor that activates nail matrix melanocytes to produce increased amounts of melanin. One exception is SCC-Bowen that might be polydactylic especially in contiguous fingers in subjects exposed to ionizing radiations. Drugs are among the most frequent causes of activation of nail matrix melanocytes. Drug-induced melanonychia usually appears 3-8 weeks after the drug intake and presents as light brown-black longitudinal or multiple transverse bands [27]. Drugs responsible for such changes include chemotherapeutic agents, hydroxyurea, psoralens, and others [28]. It is usually reversible within 6-8 weeks, although it may persist for months after withdrawal of the responsible drug. Melanonychia on multiple nails may also result from pregnancy, fungal infections, ethnic pigmentation, Laugier-Hunzkier syndrome or inflammatory disorders [27,29,30]. Whenever assessing a patient with polydactylic melanonychia, it is advised to take a detailed medical history that may help uncover the causative factor.

Similarly to what mentioned above about hemorrhage, it should be underlined that a systemic cause of polydactylic melanonychia does not exclude the possibility of melanoma. For instance, since it is well-known that ALM is the most common melanoma subtype in dark skin types, an ethnic-type pigmentation of several nails does not exclude that a melanoma or SCC might appear in one of these nails.

Step 4. Free Edge Matters

Dermatoscopic examination of the free edge of the nail plate provides additional information that might be clinically relevant. First, it allows a more precise topographic evaluation

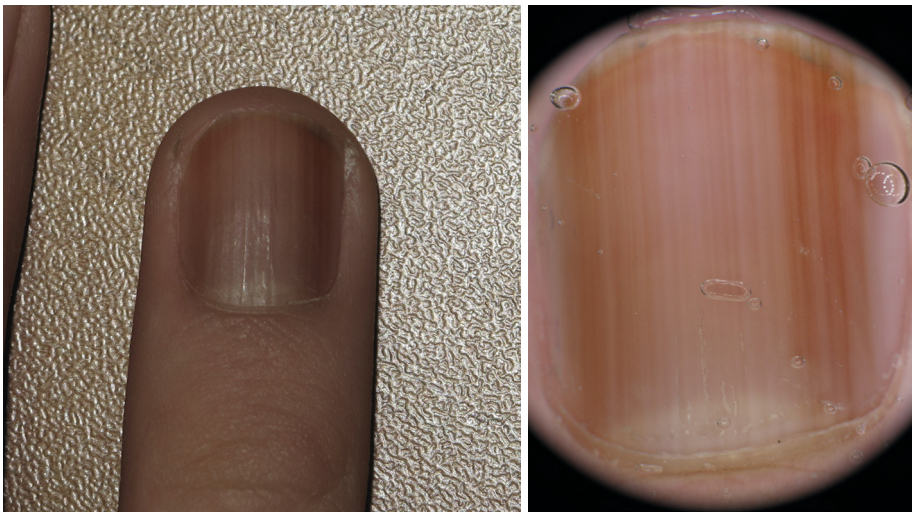

Figure 5. A 7-year old child with a nail matrix congenital nevus resulting in a melanonychia striata involving almost the entire nail plate and characterized by asymmetry of colors.

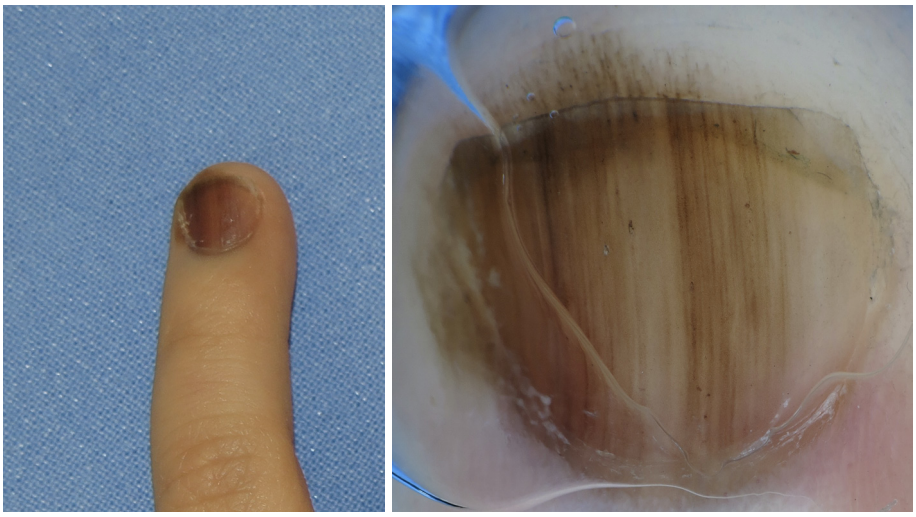

Figure 6. A 4-year old child with a nail matrix congenital nevus resulting in a highly asymmetric pigmentation of the nail plate that expands also to the skin of the lateral and distal nail fold. The pigmentation of the periungual skin of the distal nailfold is typified by a characteristic fibrillar pattern, which typically results for subungual congenital nevi.

of the pigmentation. Specifically, pigmentations involving the upper part of the nail plate probably result from a melanocytic tumor located on the proximal matrix, while those involving the lower part of the nail plate correspond to tumors of the distal matrix [31]. Second, the assessment of the free edge might reveal nail plate deformities suggestive of non-melanocytic tumors, which, occassionaly, might be pigmented. For example, detection of localized thickness changes of the free edge of the plate almost excludes "melanocytic" causes, and the presence of characteristic clues might confirm the diagnosis of a non-melanocytic tumor such as pigmented onychopapilloma, onychomatrichoma, Bowen disease or squamous cell carcinoma [32-34] (Figures 7 and 9).

Step 5. Brown or Gray?

If all the aforementioned causes have been excluded in the previous steps, the next step is to try to predict if the pigmented nail band results from proliferation (melanocytic tumor) or simple activation of nail matrix melanocytes. Although, as described above, activation of nail matrix melanocytes is usually polydactylic when resulting from a systemic cause, it might also occur in only one digit reactively to a previous trauma, infection or other local cause [35].

Discriminating between a monodactylic melanocytic activation and a nail matrix tumor is challenging and dermatoscopy might be of help. A melanocytic proliferation (benign-nevus or malignant-melanoma) usually results to a

Figure 7. Dermatoscopy of the free edge reveals a focally thinner nail plate, a hyperkeratotic plug underneath the nail plate and a punctate hemorrhage, suggestive of onychopapilloma.

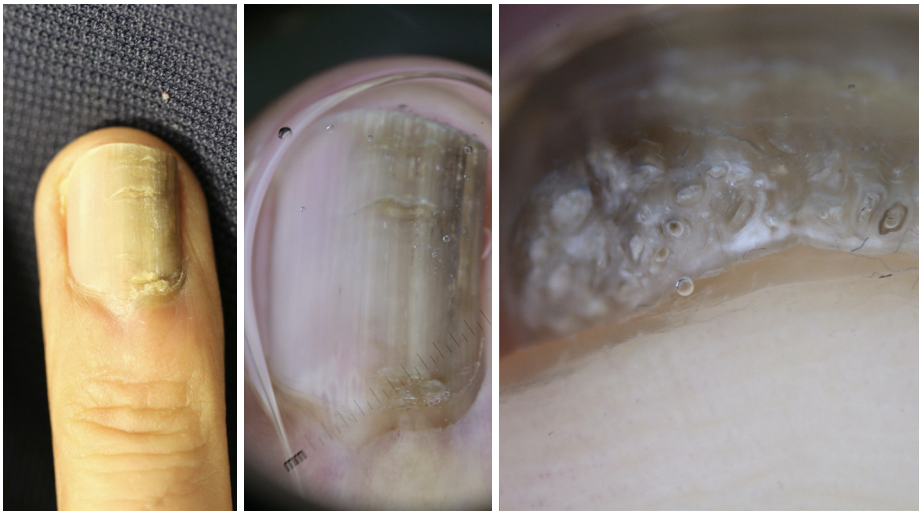

Figure 8. An onychomatrichoma typified in free edge nail plate dermatoscopy by extensive thickening of the nail plate and the characteristic nail pitting or "honeycomb pattern".

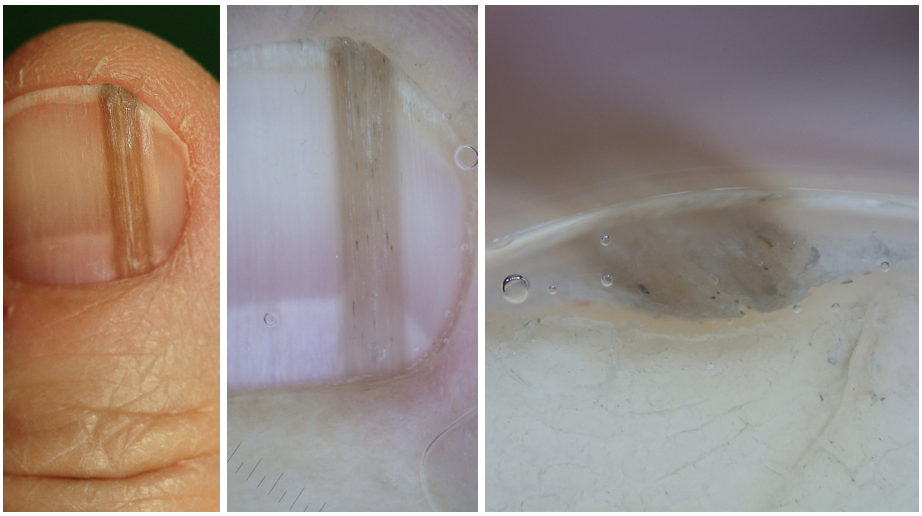

Figure 9. Free edge nail plate dermatoscopy of this squamous cell carcinoma reveals extensive localized subungual hyperkeratosis without pitting.

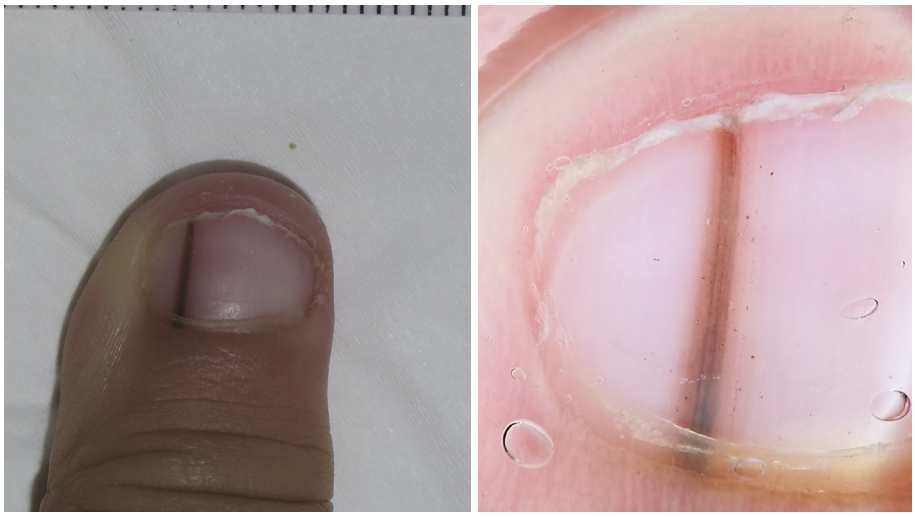

Figure 10. A brown color of the nail band is suggestive of a melanocytic tumor of the nail matrix, in this case a nevus.

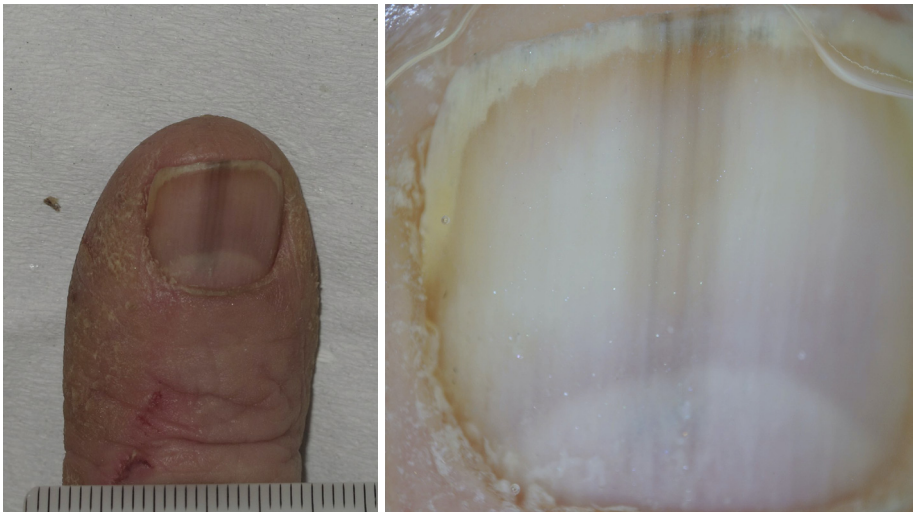

Figure 11. A gray color of the nail band is suggestive of activation of nail matrix melanocytes, in this case reactive to a previous trauma.

brown or black-colored nail band. In contrast, a gray color of the band is rather suggestive of melanocytic activation (Figure 10 and 11). In most cases lentigo of the nail matrix (isolated or in the context of a Laugier-Huntziker disease or another lentiginosis) the color is also gray.

Step 6. Size Matters

A monodactylic longitudinal melanonychia of brown-black color is probably suggestive of a melanocytic tumor on the nail matrix, either a nevus or a melanoma [1,36]. Before assessing the dermatoscopic pattern and features of the nail band, useful diagnostic information derives from its width. A retrospective observational study done by the International Dermoscopy Society [26] analyzed 82 cases of pigmented nail bands in adults and reported that an involvement of more than ⅔ of the nail plate posed an 8-fold increased probability of melanoma. It has to be emphasized that the "size" criterion should only be considered one-sided, meaning that a wide nail band is suspicious for melanoma, but a narrow band does not exclude an early and still small melanoma of the nail matrix. Obviously, the size criterion does not apply in childhood, but this was already discussed above. In terms of management, this translates into the following recommendation when evaluating a mododactylic pigmented nail band of brown-black color in adults: Wide bands (covering more than 2/3 of the surface of the nail plate should be managed with extreme caution and possibly histopathologically evaluated even if they are not particularly asymmetric, whereas smaller bands should enter the following step (Figures 12 and 13).

Step 7. Regular or Irregular?

The dermatoscopic features of pigmented nail bands resulting from nail matrix nevi and melanoma have been previously investigated [37-39]. Typically, nail matrix nevi produce a

Figure 12. Subungual nevi in adults usually result in relatively narrow nail bands that rarely involve more than 2/3 of the nail plate.

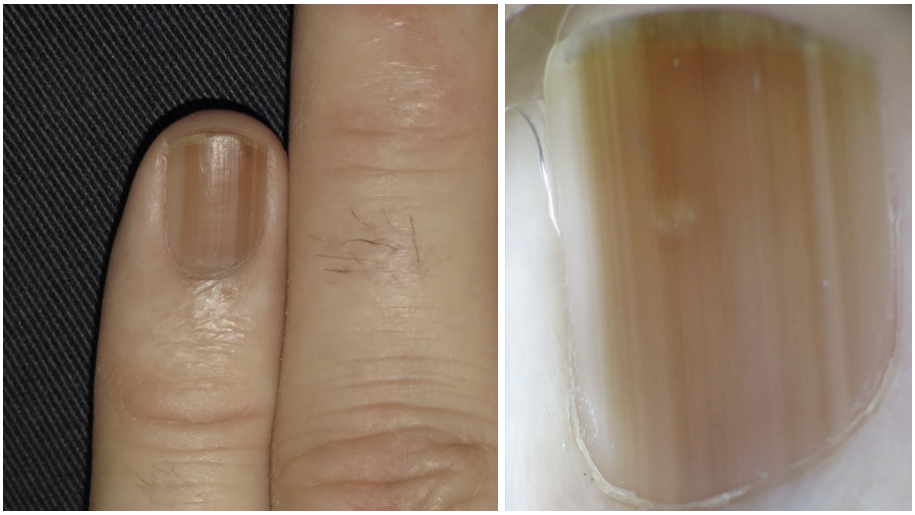

Figure 13. A melanonychia striata developing in a 55-year old woman. Although the band displays only mild asymmetry, the fact that it involves almost the entire nail plate is highly suggestive of melanoma.

relatively homogeneous band in terms of color that might vary from light brown to dark brown or black. In contrast, a pigmented nail band resulting from nail matrix melanoma is more likely irregular, consisting of parallel lines of variable width and variable shades of brown, gray or black color (Figure 14). Additional features are the presence of granular pigmentation and the expansion of the pigmentation on the periungual skin of the proximal or lateral nail folds (Figure 15) that might visible macroscopically (Hutchinson sign) or only dermatoscopically (micro-Hutchinson sign) [14,38-41]. At a more advanced stage, melanoma may also cause nail dystrophy and splitting of the nail bed (Figure 16). The presence of one or more of the above dermatoscopic features should raise the suspicion of melanoma and probably warrants biopsy and histopathologic examination. In contrast, homogeneous and narrow nail bands can be safely monitored, taking into consideration also the last step below.

The Last Step: Follow-up or Follow-back?

Sequential follow up with digital dermatoscopic images is commonly used in daily practice and was shown to be particularly useful when appropriately applied. This is because it provides robust information on the natural biologic evolution of lesions and, therefore, enables the recognition of early featureless melanoma while helping to reduce the excision rate of benign lesions [42,43]. For the assessment of pigmented nail bands, follow-up is particularly helpful for several reasons. First, as discussed above, obtaining biopsies from the nail matrix is technically much more demanding as compared to other anatomic sites. Second, early melanoma

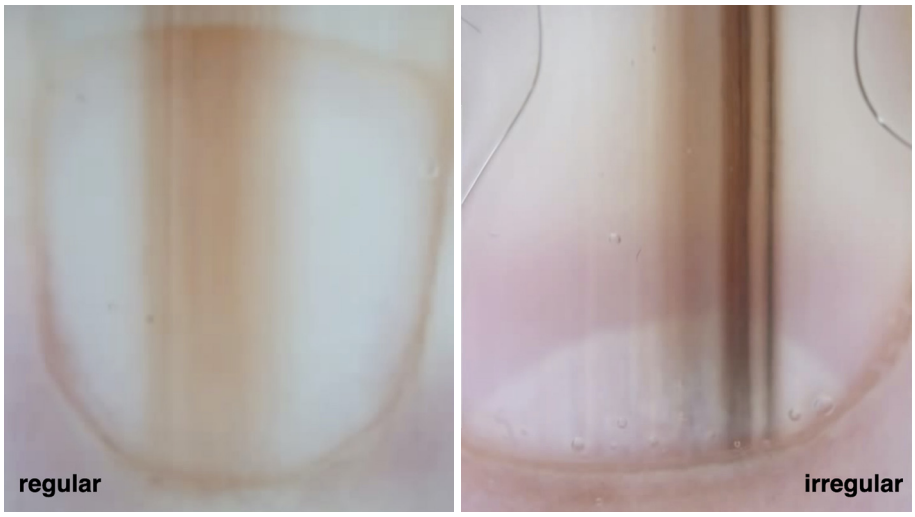

Figure 14. A uniform in color pigmented nail band on the left (nevus) and an asymmetric nail band on the right, consisting of internal lines of different color and thickness (melanoma).

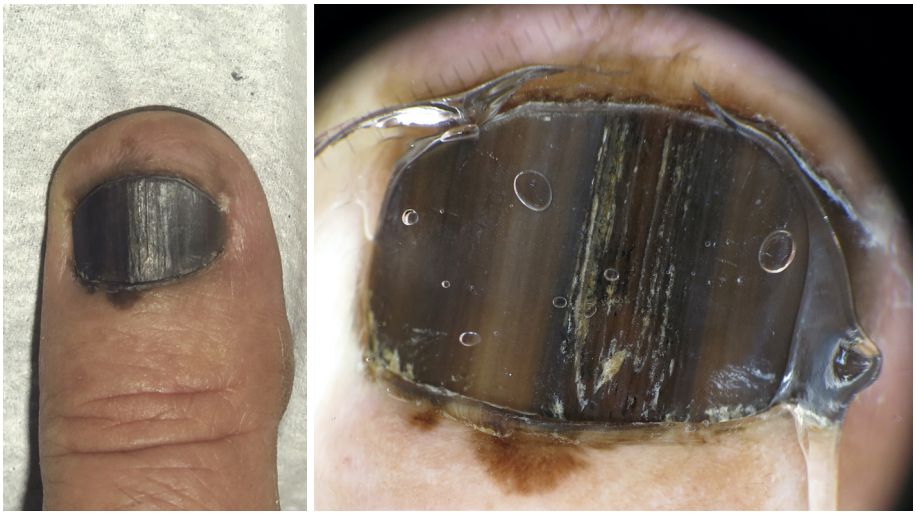

Figure 15. The expansion of pigmentation in the periungual skin (Hutchinson sign) is almost always suggestive of melanoma in adults.

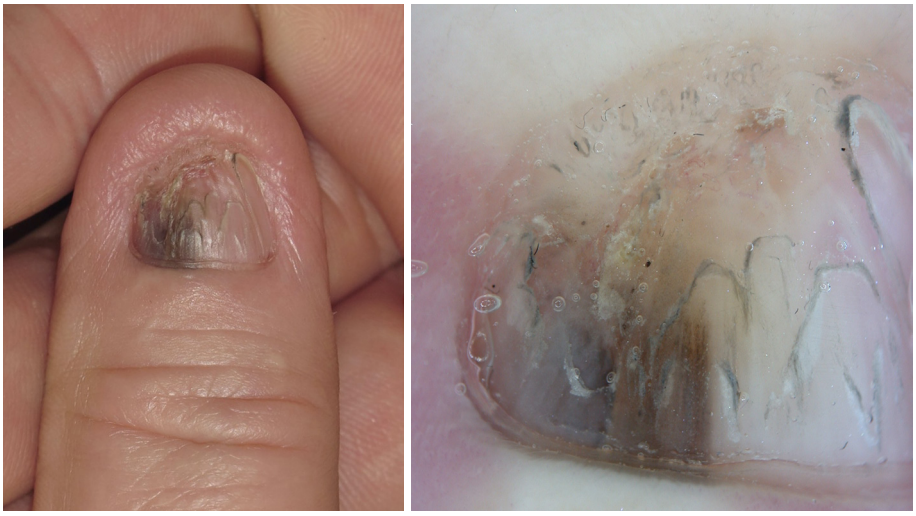

Figure 16. Onychodystrophy and nail plate loss in a melanoma.

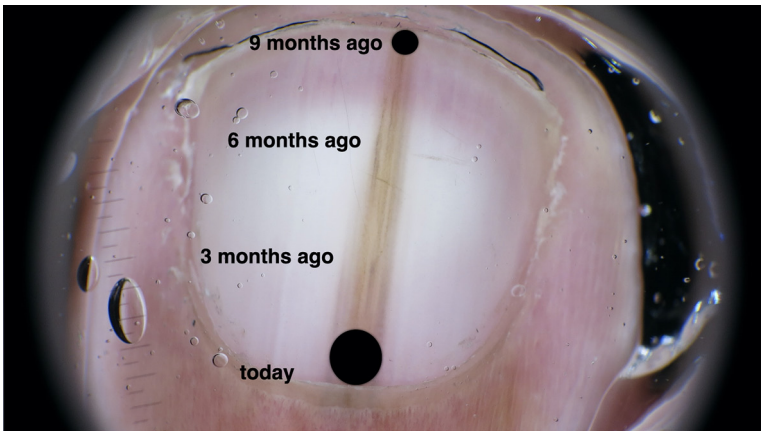

Figure 17. Dermatoscopic examination of the nail plate with a melanonychia striata reveals the evolution dynamic within a timeline of a few months back.

might display only bland histopathologic features and perfoming biopsy of melanomas at a very early stage might results in inconclusive or false negative histopathology assessments [11,25,44]. Third, after inconclusive biopsy of a melanonychia striata, dermoscopy follow-up becomes very difficult since the scar in the matrix (even after a shave biopsy) creates irregular patent of the possible recurrent pigmentation. Fourth, the presence of blood or other substances (ex. keratin) might impede the complete visualization of the nail plate at the baseline visit. In fact, in the current document, follow up has been recommended in several scenarios (eg hemorrhage, nevi in children, narrow homogeneous bands in adults).

The main limitation of this strategy is the obvious need for multiple examinations at different time points, which depends on time availability and patients compliance. Interestingly, for pigmented nail bands resulting from nail matrix tumors, information about the evolution of the lesion is already provided by a careful baseline examination. This is because the nail plate gets pigmented when it is still in the matrix because of the underlying tumor but then moves distally and remains visible for several months, until reaching the distal nail fold. This means that, observing the distal part of a pigmented nail band provides information on the size of the nail matrix tumor some months earlier. The precise timing depends on the age, since the growth rate of the nails varies by age [45]. Therefore, a pigmented nail band that is wider proximally and narrower distally (triangular shape), corresponds to a nail matrix tumor that was smaller some months ago as compared to today (Figure 17). This unique type of "follow back" is available at all nail plate examinations and provides useful information on the growth rate of the nail matrix tumor that should integrated in the overall evaluation and according to the patient age.

This study is only conceptual and opinion-based. The review of the literature was not performed with a systematic methodology and all the suggested recommendations should be interpreted critically.

Conclusions

In this 7-step + 1 approach, we attempted to incorporate available evidence on assessment of melanonychia striata, addressing important issues that influence clinical decision-making and diagnostic procedures.

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