Review Article

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Basic approach to melanonychia: a review

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ABSTRACT

Melanonychia is a brownish-black staining of the nail plate. It can affect a single or several nails on both the fingers and toes. Melanocytic activation and melanocytic hyperplasia are the two basic mechanisms involved in the development of melanonychia. Melanocytic activation occurs as enhanced melanic pigmentation of the nail matrix epithelium and nail plate without a corresponding rise in the number of melanocytes, resulting in melanonychia. The number of matrix melanocytes increases in melanocytic hyperplasia. Involvement of a pathogen has also been suggested as a mechanism for its development. A thorough clinical history should be taken, including questions regarding various triggers and causal events, as well as the use of a questionnaire. A proper detailed physical examination is of a great need to properly identify the type of melanonychia and to rule out melanoma which is of great importance in clinical practice. Onychoscopy and nail biopsy also acts as an aid in proper diagnosis of melanonychia. Treatment of melanonychia basically depends on the underlying etiology. One major aim is to rule out melanoma if present and its proper management in time.

Keywords: Melanoma, Melanocytic activation, Melanocytic hyperplasia, Onychoscopy, Biopsy

INTRODUCTION

Melanonychia is derived from the Greek words "melas," which means "black" (or "brown colour") and "onyx," which means "nail." It is distinguished by brown-black staining of the nail plate, with melanin as the pigment in question. It might affect a single or several nails on both fingers and toes.¹ Melanonychia is the most common cause of chromonychia, accounting for about half of all cases.¹

The most prevalent morphological feature is longitudinal melanonychia, which starts at the matrix and extends to the tip of the nail plate. Pigmentation can affect the entire nail plate (complete melanonychia) or appear as a transverse band in other cases (transverse melanonychia). Transverse melanonychia and total melanonychia are substantially less common.

PATHOGENESIS

Two main mechanisms are involved in the appearance of melanonychia, melanocytic activation and melanocytic hyperplasia.² The distinction between the two can be made based on the medical history of the patient, the clinical picture, dermoscopy and histopathological examination and is essential for the adequate management of the patient.²

Melanocytic activation

Melanocytic activation (also termed melanocytic stimulation or functional melanonychia) describes the process by which melanonychia results from increased melanic pigmentation of the nail matrix epithelium and nail plate without a concurrent increase in the number of melanocytes.³ Seventy-three percent of adult cases of

single digit longitudinal melanonychia (LM) occur as a result of melanocytic activation.^{3,4} Several physiologic, local and regional, dermatologic, systemic, iatrogenic, and syndromic factors may lead to melanocytic activation.^{2,5}

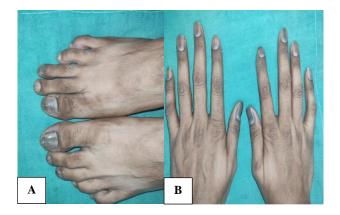


Figure 1 (A and B): Case of racial melanonychia presented to dermatology OPD.

Melanocytic activation include: physiologic causes such as racial melanonychia and pregnancy; local and regional causes such as repeated local trauma from poor footwear or overriding toes, onychotillomania, nail biting, occupational trauma and carpal tunnel syndrome; dermatologic causes such as onychomycosis, chronic paronychia, and psoriasis; lichen planus such as myloidosis, chronic radiation dermatitis, systemic lupus erythematosus, localized scleroderma, onychomatricoma, Bowen's disease, myxoid pseudocyst, basal cell carcinoma, subungual fibrous histiocytoma, verruca vulgaris, and subungual linear keratosis; systemic causes such as endocrine disorders (Addison's disease, Cushing's syndrome, Nelson's syndrome, hyperthyroidism and alkaptonuria, nutritional acromegaly), disorders. hemosiderosis, hyperbilirubinemia, porphyria, graft versus host disease (lichen planus-type changes accompanied by longitudinal melanonychia) and AIDS; iatrogenic causes such as phototherapy, X-ray exposure, electron beam therapy and drug intake.3,6,7

Melanocytic hyperplasia

The 2nd broad category of melanonychia, melanocytic hyperplasia, is characterized by an increase in the number of matrix melanocytes.³ Both benign and malignant forms exist.³ Benign melanocytic hyperplasia is subdivided into 2 categories, lentigines, when nests of melanocytes are absent and nevi, when at least 1 melanocytic nest is present.³ While lentigines are observed more often than nevi in adults, nevi are found far more often than lentigines in children. NAM occurs rarely in children, and benign melanocytic hyperplasia constitutes 77.5% of cases of childhood melanonychia.^{2,8}

Malignant melanocytic hyperplasia includes both *in situ* and invasive melanoma of the nail apparatus.³ Melanoma is most commonly observed in the thumbs,

index fingers and great toes in patients mean age 60-70 years.³

Melanocytic hyperplasia is divided into lentigo, nevus (congenital nevi and acquired nevi) and nail apparatus *in situ* and invasive melanoma.

Pathogen induced melanonychia

As previously highlighted, certain pathogens involved in onychomycosis or paronychia can trigger an inflammatory response that induces melanocytic activation resulting in melanonychia. In addition, some gram-negative bacterial pathogens such as *Proteus mirabilis* and some dermatophyte strains, such as *Trichophyton rubrum* var. *nigricans*, can produce melanin and infrequently present as a linear streak.^{6,9} Several other organisms can present with linear brown-to-black nail dyschromia by producing a pigment other than melanin.

EVALUATION OF MELANONYCHIA

History

A detailed history should be taken including patient's age, history of trauma/any triggering factor, exogenous substance exposure, occupational history, hobbies, drug history, medical and family history. The onset (gradual/sudden), duration (short/long), rate of progression of melanonychia and change in color or width of band must be enquired.¹

Providing patients with a nail questionnaire with inquiries concerning their occupation, hobbies, exposure to topical substances, history of digital trauma, drug history, medical history and family history prior to the visit allows them ample time to prepare thoughtful answers, and also allows the physician more time during the appointment to focus on key portions of the history.

Nail apparatus melanoma should be suspected in any patient with unexplained melanonychia who provides a history containing any of the following features: involvement of a single digit (especially the thumb, index finger, or great toe); development during the fourth decade of life or later; development in the setting of a history of digital trauma; development in the setting of a personal/family history of melanoma or dysplastic nevus syndrome; development in the setting of nail dystrophy; and abrupt development or change (darkening or widening proximally).^{3,6,7,10}

Physical examination

Initial physical examination should include evaluation of all twenty nails, skin and mucous membranes while keeping in mind all potential causes of brown-to-black nail pigmentation. Questions to help guide the initial examination of the nails include the following: are one or more nails involved? If multiple nails are involved, is one particular nail changing or different from the rest? Is the discoloration located on top of, within, or beneath the nail plate? Is the discoloration linear in orientation? Is the band wider or darker proximally? Is the discoloration associated with nail plate dystrophy?

One should note the following parameters.

Number and location of involved nails

Single/multiple nails must be observed.

Morphology of LM

It is seen whether similar or different and if multiple nails were involved.

Site or location of melanonychia on the nail plate

It is observed if the site is above, within or beneath. Examination of the distal free edge of the nail plate or hyponychium might indicate the origin of pigment. Ventral nail plate pigmentation originates from the distal matrix while the dorsal nail plate from proximal matrix.²¹

The localization of pigment helps in selecting the anatomic site for exploration and biopsy, and can prevent a visible definitive nail dystrophy if the surgery is confined to the distal matrix.²¹

Pattern of melanonychia

Pattern of melanonychia is observed-complete, longitudinal or transverse.

Complete melanonychia

The extent and configuration (proximal and distal end including shape of proximal end of pigmentation with respect to proximal nail fold) must be observed.

LM

LM must be noted-color, homogeneity, regularity, width, whether wider proximally or distally, shape, margins and lateral borders of the band. Pyramid-shaped melanonychia with base toward proximal nail fold is suggestive of NUM.

Other nail signs

Other nail signs such as nail dystrophy, nail plate changes (abrasion, splitting or fissuring) and periungual pigmentation, bleeding are pointers to NUM. In addition, nail dystrophy and nail plate changes and pigmentation may be seen in fungal melanonychia.

Other mucocutaneous sites for any inflammatory disorders, syndromic associations must be noted.

ABCDEF rule

The ABCDEF rule helps to distinguish alarming LM from the nonalarming ones.¹¹

Table 1: The ABCDEF rule in LM.

Letter	The ABCDEF rule in LM
A	Age, Afro-Americans, native Americans, and Asians): 5th and 7th decades
В	Nail band: brown to black colour, $\geq 3 \text{ mm}$ wide, irregular borders
С	Change: rapid ↑ in size of band and/or change in morphology
D	Digit involved: thumb >hallux >index finger, dominant hand, single digit
Е	Extension: Hutchinson's sign
F	Family: personal or familial history of nevi dysplastic syndrome and melanoma

Laboratory evaluation

Nail plate sampling by nail clipping or punch biopsy can be done in doubtful cases about the nature of the pigment and in cases suspicious of fungal melanonychia.⁵ The samples are sent for direct microscopy and culture (to exclude onychomycosis) and for histopathology (to confirm melanic pigmentation by Fontana stain).⁵

Hutchinson's sign

The surrounding skin should be carefully examined for discoloration similar to that seen in the nail plate. Hutchinson's sign, or the extension of pigment from the matrix to the perionychium in association with NAM is sometimes helpful in confirming the clinical diagnosis but is an inconsistent feature.¹⁰ Melanoma can occur without Hutchinson's sign. Moreover, pseudo-Hutchinson's sign, or the presence or illusion of pigment in the perionychium, is associated with both benign and malignant conditions in the absence of melanoma.^{3,10,12}

Dermoscopy (onychoscopy)

When performed by trained examiners, dermoscopy has already proven its efficiency in the differential diagnosis of cutaneous pigmented tumors. The main difficulty in the evaluation of nail pigmentation is that the lesions that are examined with dermoscopy correspond to melanin deposition in the nail plate and not to the site of melanin production, which is in the nail matrix or in the nail bed. Intraoperative nail matrix dermoscopy permits more accurate diagnosis but it is an invasive procedure that cannot be used routinely.

Dermoscopy also has been proposed before surgery to select the anatomic site to be explored. Examination of the distal edge of the nail establishes the localization of pigment within the nail plate and then which part of the matrix is involved. Pigmentation of the lower nail plate corresponds to a distal nail matrix origin, and pigmentation of the higher nail plate corresponds to a proximal localization of responsible melanocytes. In most cases of melanonychia, the pigment is in the lower (ventral) part of the nail plate as most bands originate from the distal matrix.¹³

Nail plate dermoscopy

Dermoscopy of the nail plate always requires oil or gel immersion because of the convex shape of the nail. Dermoscopic patterns for evaluation of nail pigmentation have been described but their accuracy in the diagnosis of subungual melanoma has not been established.¹⁴⁻¹⁷ Similarly, there are no evidence-based studies to in- form the clinician as to the frequency of dermoscopic follow-up in patients with melanonychia. There are no precise dermoscopic criteria that can be used to decide when to biopsy the lesion. Dermoscopy of the nail plate permits differential diagnosis between non- melanocytic and melanocytic pigmentation and may permit differential diagnosis between nail matrix melanocyte activation and hyperplasia but should not be considered a substitute for pathology in the differential diagnosis of longitudinal melanonychia.20

Dermoscopic patterns that suggest subungual hematoma

Irregularly-shaped purple to brown-black areas with round, dark red spots at the periphery and a "filamentous" distal end are patterns that have been associated with subungual hematomas. However, we should remember that the presence of blood extravasation does not exclude an associated melanoma.²⁰

Dermoscopic patterns that suggest a diagnosis of melanocyte activation

A gray background with thin gray regular parallel lines suggests melanonychia due to nail matrix melanocyte activation. In traumatic melanocyte activation, tiny dark red to brown spots corresponding to blood extravasation may also be seen.²⁰

Dermoscopic patterns that suggest a diagnosis of nevus

The presence of a brown background with longitudinal brown to black regular parallel lines often suggests a nevus. In children, black dots (less than 0.1 mm) similar to those described in skin melanocytic lesions are frequently observed and correspond to pigment accumulation in the nail plate.²⁰

Dermoscopic patterns that suggest a diagnosis of melanoma

Brown background with longitudinal, brown to black lines with irregular coloration, spacing or thickness and parallelism disruption suggest melanoma. Dermoscopy also can be used to detect Hutchinson's sign before clinical detection by unaided visual inspection. Dermoscopy of eroded nodules of the nail bed often permits detection of peripheral pigmentation in amelanotic melanoma, allowing differential diagnosis from pyogenic granuloma and non-melanocytic nail tumors.²⁰

Nail matrix dermoscopy

Intraoperative dermoscopy permits direct visualization of the site of melanin production in the nail bed or matrix with patterns that are similar to those found in skin melanocytic lesions. Dermoscopy of the nail bed and matrix is also very useful to select the surgical margins, and may avoid omission of small pigment foci.^{18,19}

Nail biopsy

As the clinical diagnosis of melanonychia is frequently difficult, a biopsy is oftentimes necessary to rule out melanoma.⁷ In fact, a study by Di Chiacchio et al found that the overall accuracy of dermatologists in the preoperative diagnosis of NAM *in situ* was low ranging from 46-55%.²¹ Interestingly, the study also found that a dermatologist's level of expertise in nail disease did not statistically influence the correct diagnosis.²¹

While no formally adopted algorithm with guidelines for when to perform a diagnostic biopsy exists, there are several suggested clinical practices that help guide clinical decision making.¹⁰ The threshold for biopsy should be low in a white patient with unexplained melanonychia of a single digit.^{3,22} For cases of unexplained melanonychia of a single digit in a nonwhite patient, or of multiple digits in a patient with any phototype, melanonychia should be closely monitored and biopsied if any suspicious features arise.^{3,22} Because unexplained melanonychia in children is rarely due to an underlying melanoma, their management is more conservative.^{3,21}

When performing a biopsy, the origin of the pigment, which most often lies in the nail matrix, should be sampled in its entirety. The nail matrix biopsy, while a relatively safe and simple procedure when basic principles are followed, is associated with the greatest risk in terms of scarring when compared to other biopsy locations within the nail unit. With regards to the anatomy and physiology of the nail unit, the distal matrix forms the ventral nail plate, and the proximal matrix forms the dorsal nail plate.^{10,23-25} Thus a biopsy of the distal matrix is almost always preferred over a proximal matrix biopsy as any resultant scar, which clinically manifests as a thinned ridge, would lie on the undersurface of the nail plate.^{10,23-} ²⁵ Thinned ridges on the dorsal surface of the nail plate are easily traumatized as they catch on items such as clothing and are much more troublesome for the patient.¹⁰

In order to minimize any potential scarring, nail matrix excisional biopsies can be oriented transversely.^{7,10,23} Moreover, full thickness nail matrix biopsies larger than

3 mm can be sutured in order to achieve an optimal cosmetic result. $^{1,26}\!$

The punch biopsy is generally reserved for longitudinal melanonychia less than 2.5–3 mm in width originating in the distal matrix.^{6,7} A punch biopsy should be taken at the origin of the pigmented band and should extend to depth of the periosteum.^{7,23} Punch biopsies are generally not recommended for evaluating pigmented lesions 3 mm or more in width (even if multiple punch biopsies are taken) because peripheral pigmentation may not be adequately sampled to rule out malignancy. Additionally, taking serial punch biopsies is associated with an increased risk of permanent nail dystrophy.⁷

The lateral longitudinal excision is best suited for biopsying suspicious lesions located in the lateral onethird of the nail as this technique samples all components of the nail unit including the nail matrix, nail bed, nail fold, and hyponychium.^{6,7} The tangential (shave) excision is ideal for sampling a longitudinal pigmented band with a lower preoperative suspicion of melanoma that is greater than 3 mm in width in the midnail plate or of any width originating in the proximal matrix.^{6,7,27} The tangential technique, first described by Eckart Haneke in 1999, is less invasive than a transversely-oriented matrix excision, and it is associated with minimal long-term dystrophy despite the increased width commonly associated with its use.6,7,27 However, for any case with a high preoperative likelihood of invasive melanoma, a full-thickness nail matrix biopsy is necessary for prognosis determination as a tangential biopsy may not provide an accurate Breslow depth.⁷

On histologic examination, LM can reveal melanocytic activation, which means melanin hyperpigmentation without any increase in the number of melanocytes.

Benign melanocytic hyperplasia, which means: a benign increase in the number of melanocytes. Benign melanocytic hyperplasia can be called lentigo when melanocytes remain arranged in individual units. It is called a nevus when at least one nest is observed.

It is also defined as atypical intraepithelial melanocytic hyperplasia.

In situ melanoma characterized by an increased number of atypical melanocytes in the matrix epithelium. Most of the cells are single and located near the dermoepidermal junction. Usually, however, some tumor cells can be found in the upper layers of the epithelium. Melanocytes are both spindle and rounded, and some have long, heavily pigmented dendrites. Atypia is usually evident in the center of the lesion, while they may be only slight and focal at the periphery. Atypical intraepithelial melanocytic hyperplasia.

Clinical signs that suggest immediate excisional biopsy of the pigmentation to exclude nail melanoma are- lack of homogeneity of the pigmentation, with bands or lines of different color; presence of nail plate fissuring or splitting; proximal part of the band broader than the distal (triangular shape); blurred lateral borders of the band; and pigmentation of the periungual skin (Hutchinson's sign).

DIFFERENTIAL DIAGNOSIS

Black nail

Nail pigmentation can be a result of pigments other than melanin. Hematoma is the main differential diagnosis.²⁸⁻³¹ The patient is not always aware of a prior trauma, because it may be minor and chronic (rubbing in a sports shoe). In most cases, it grows out with the nail plate, showing a proximal border that reproduces the shape of the lunula. Rarely hematoma may not migrate because the trauma is repeated daily. However, extended non migrating hematoma should be considered as suspicious. Trauma has been evoked in the pathogenesis of melanoma, and hematoma could hide an underlying melanoma. One should not hesitate to punch a hole in the nail plate. This allows visualization of the underlying nail bed and confirmation of the nature of the pigment.

Pseudomonas and *Proteus* species have been reported to cause black nails.²⁸ Some strains of Pseudomonas produce pyocyanin (dark green) and fluorescein (yellow-green) pigments, which are responsible for nail discoloration. In histologic sections, a diffuse yellowish to brown discoloration can be seen.

Systemic medication such as clofazimine, tetracycline, gold salts, and antimalarials can provoke a dark nail pigmentation not related to stimulation of melanin synthesis.^{28,32} With clofazimine and gold salts, the color could be due to the deposition of medication in the nail plate.

In cases where the deposit is subungual, the pigmentation will not move as the nail grows, and it is often associated with pigmentation of the skin and mucosa. Minocycline induced nail pigmentation is possibly due to dermal deposition of an iron chelate of the drug. Antimalarials can give a similar pattern of pigmentation, and drug discontinuation leads to a decrease in the intensity of pigmentation that does not usually resolve completely. As with internal causes, discoloration follows the shape of the lunula.

Exogenous pigmentation can be due to topical application, such as potassium permanganate and silver nitrate. In this case, discoloration follows the shape of the proximal nail fold. It can usually be scraped off the nail surface.²⁸

In subungual linear keratotic melanonychia, the pigmented band consisting of a subungual keratinized epithelial ridge originates in the nail bed. The origin of the melanin pigment is linked to its synthesis within the acanthoma. The lesions are reminiscent of pigmented seborrheic keratosis.³³

Pseudo-Hutchinson's signs

Hutchinson's sign is an important presumptive clue to the diagnosis of subungual melanoma. There are, however, exceptions to consider when evaluating a patient suspected of having a subungual melanoma. The possibility of pseudo-Hutchinson's variants must be kept in mind to avoid over diagnosing a malignancy. They can be subdivided into benign, nonmelanoma, and illusory.¹²

Benign conditions can be associated with pigmentation of the tissues surrounding the nail plate. This can be seen in racial melanonychia, Laugier-Hunziker and Peutz-Jeghers syndromes, radiation therapy, malnutrition, minocycline, AIDS patients, congenital nevus, and regressing nevoid melanosis in childhood. It can be trauma induced by friction, nail biting and picking, and boxing. Nonmelanoma tumors, such as Bowen's disease of the nail unit, can exhibit periungual hyperpigmentation and features clinically typical of subungual melanoma.¹²

Pseudo-Hutchinson's sign can be illusory. Pigmentation confined to the nail bed and matrix can shine through the transparency of the cuticle. Rarely blood from a subungual hematoma can spread to the nail folds and hyponychial areas.¹²

Differential diagnosis according to presentation

Differential diagnosis according to presentation include: non-melanin pigmentation-the first and essential step is to establish the melanin or nonmelanin (e.g. exogenous, infections, hematoma) etiology; multiple nail involvement-racial, systemic causes, or frictional; single nail explained by skin and nail diseases-trauma, inflammatory disorders, or tumors; LM in children-nail matrix nevus, regular follow ups required; and LM in adults-histopathology may be needed if doubtful.³⁴

TREATMENT

Treatment of melanonychia depends on the underlying cause. The treatment of associated systemic or locoregional disease, withdrawal of offending drug, avoidance of trauma, treatment of infections or correction of nutritional deficiencies may cause regression of pigmentation. Benign causes do not necessitate treatment and can be kept in follow up. Depending on thickness and histopathological characteristics, subungual melanoma may be managed by functional surgical treatment (wide local excision) or digit amputation with or without sentinel lymph node mapping/biopsy.³⁵

CONCLUSION

There is a need for a reassessment in the approach to accurate diagnosis and management of melanonychia. This review is being conducted to provide a basic approach to a proper understanding of melanonychia, the basic pathophysiology in its development, proper measures taken in its diagnosis, sufficient management, and, most importantly, to rule out the presence of melanoma and its timely management

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