Evaluation of Pigmented Lesions of the Nail Unit

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Acquired pigmentary changes of the nail are secondary to a number of etiologies. These include nail matrix nevi; physical induction secondary to trauma; malignant melanoma; nutritional deficiencies; inflammation secondary to lichen planus; endocrine causes such as Addison's disease; or secondary to bacterial, fungal, or viral infections. The most important task faced by clinicians is to distinguish benign from malignant etiologies of nail pigmentation. We will briefly review the various entities that can yield dyspigmentation and their differentiation from melanoma of the nail.

There are multiple causes of pigmentary changes of the nail unit. They can affect singular or multiple fingernails. The clinical appearance of color changes in the nail is dependent on several variables. These include the nail's thickness and its attachment to underlying tissues.[1] Pigmentation caused by exogenous topical agents corresponds to the shape of the nail fold. By contrast, pigmentary changes due to endogenous systemic causes affect the nail matrix and correspond to the shape of the lunula.[1] If there has been a lapse between the occurrence of the stain or trauma and the presentation to the clinician, there will be a margin of clean nail that corresponds to the longitudinal nail growth achieved in the interim. This review will focus on the evaluation of pigmented nail disorders and the workup for subungual melanoma.

Longitudinal Melanonychia

Longitudinal melanonychia (LM)(Figures 1 and 2), which manifests clinically as pigmented longitudinal striations of the nail bed, shows significant relevant racial differences. LM is rare in fair-skinned individuals, affects 15% to 20% of Asian people, and is common in African Americans.[2] LM can be melanocytic in origin or nonmelanocytic. Melanocytic activation can be secondary to melanocyte hyperplasia. Nail matrix nevi are identified histologically by focal melanin accumulation at the dermoepidermal junction.[3] LM can also be the end result of repeated nail trauma, such as in children who bite their nails. Nonmelanocytic origins of melanonychia include nutritional deficiency, such as the blue striae in patients with megaloblastic anemia. Infection with *Pseudomonas aeruginosa* can yield a greenish black deposition. Other infectious causes of pigmentary deposition include *Trichophyton rubrum* and *Aspergillus niger*. It also is seen in patients with HIV.

Figure 1. Longitudinal melanonychia of fingernails.

Intensely pigmented melanonychia due to congenital or acquired nevi occur principally in children or young adults. They are readily recognized histologically and may be associated with a pseudo-Hutchinson's sign (a periungual deposition of pigment in the overlying transparent cuticle in association with a benign lesion). In a new pigmented lesion with an uncertain history of preceding trauma, melanoma must be ruled out. In a recent review of

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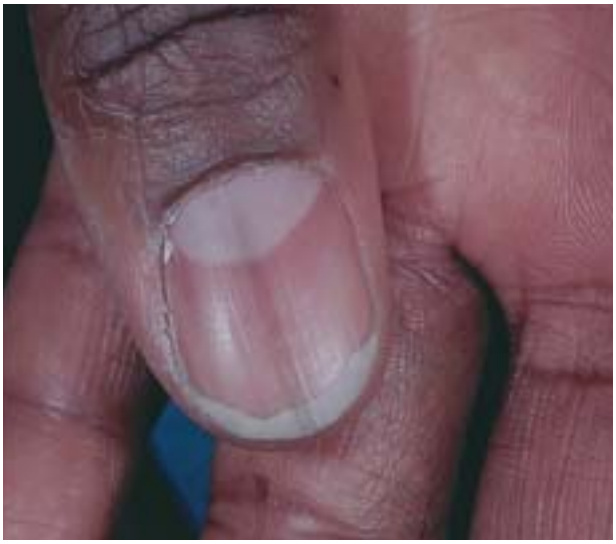

Figure 2. Close-up view of longitudinal melanonychia.

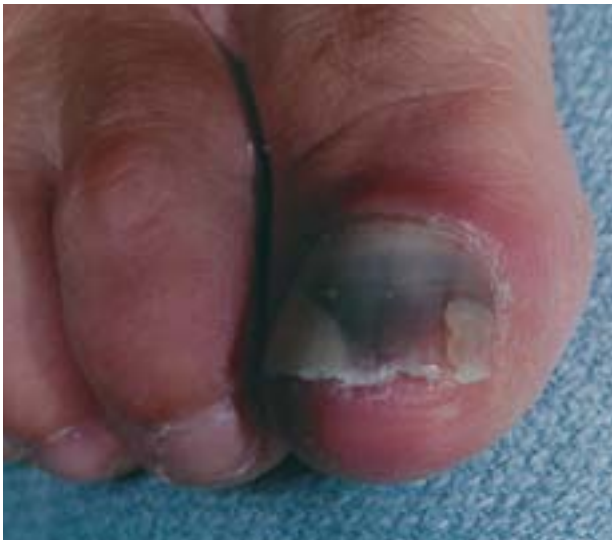

Figure 3. Subungual hematoma secondary to trauma.

nail matrix nevi, Tosti et al[4] reported on the prevalence of nail matrix nevi. Toward this end, they performed nail biopsies on 100 white patients with a single band of idiopathic LM. They found nail matrix nevi in 22 patients and concluded that "nail matrix nevi are uncommon but not exceptional."[4]

Nail matrix nevi are more common in fingernails than toenails; half of all cases involve the thumb. The size and degree of pigmentation varies considerably. In most cases, the nevus produces a heavily pigmented band that can strongly simulate a melanoma.[4] They also can undergo spontaneous involution.[5] Diagnosis of a nail matrix nevus requires histological examination, as it cannot be differentiated from melanoma clinically. As a consequence, it is the accepted standard of care that any patient with LM involving only one nail and not clearly related to any other etiology should have a nail biopsy performed.

The most important clinical decision is establishing whether the nail pigment represents a malignancy. Melanoma of the nail unit, barring appropriate clinical history and findings, must always be ruled out. Biopsy of the nail matrix and nail bed in persistent lesions is a necessity, particularly in white patients. Conclusive diagnosis can be made only pathologically. Management must include, at a minimum, complete excision of the lesion. In nonmalignant etiologies, removal of the causative agent can yield improvement for those melanonychia due to drug eruptions. Antimycotics or antibiotics can be used to treat infectious etiologies.

Hutchinson's Sign

Hutchinson's sign, an important clue to the diagnosis of subungual melanoma, is defined as periungual extension of brown-black pigment from LM of the nail bed, matrix, and nail plate onto the proximal and lateral nail folds and cuticle. It can present as a dark circle or a large dot. When accompanied by ulceration of the nail bed or obliteration of the nail plate with a tumor, it is essentially pathognomonic of subungual melanoma.[6] It represents the radial growth phase of subungual melanoma.[7] However, the mere presence of the pigment is not pathognomonic of subungual melanoma.

There are 3 exceptions to the Hutchinson's sign rule. Proper recognition of these situations will help the clinician to diagnose a true Hutchinson's sign as opposed to a pseudosign suggesting a different etiology. The first of the 3 exceptions are those benign conditions such as trauma, use of minocycline, and the presence of a congenital nevus. In all examples, single or multiple nails are associated with periungual hyperpigmentation.[6] The second exception, as described by Sau et al,[8] is Bowen's disease of the nail unit, which can present with a pseudo-Hutchinson's sign. The third is what is termed the *illusory appearance* of Hutchinson's sign.[9] This occurs when benign disorders, such as subungual hematomas secondary to trauma (Figure 3) and melanocytic nevi, produce pigment that is confined exclusively to the nail matrix and bed. The physiological reason that the illusion appears is that the nail fold and cuticular tissue are transparent; therefore, the brown-black pigmentation appears to be emanating from that area when it is actually arising from the matrix. Another factor complicating proper diagnosis is the relatively high prevalence of subungual melanoma of the amelanotic variety, which, by definition, would not present with a Hutchinson's sign.

Each of these examples represents a case of periungual hyperpigmentation in association with an LM

streak and can be misleading for even the astute clinician. Indeed, the absence of periungual pigmentation (a negative Hutchinson's sign) does not preclude the diagnosis of subungual melanoma.[6] Clinicians must inquire carefully regarding the history of the lesion, recent drug ingestions, past treatment, hobbies, and occupational exposures.

Diagnosis of Subungual Melanoma

Recently, Levitt et al[10] reviewed the clinical detection of subungual melanoma and proposed the application of a systematized approach to pigmented lesions of the nail. Applying this method greatly simplifies the approach to the relatively rare presentation of subungual melanoma. Levitt et al[10] suggested the following ABCDEF approach for diagnosis of subungual melanoma: *A* refers to age with a peak incidence in the fifth to seventh decades, particularly in African American and American Indian patients. *B* refers to band, breadth, and border; the band is brown-black with a breadth of greater than 3 mm and an irregular border. C stands for change (or the lack thereof); the clinician must be concerned with a rapid increase in size of a pigmented lesion, as well as a lack of change after an appropriate course of therapy. *D* represents the digit involved, with the thumb being the most worrisome; single digits are more alarming than multiple ones. *E* refers to the extension of pigment to involve the lateral nail fold (true Hutchinson's sign). *F* is a family history of previous melanoma or dysplastic nevi.[10] This systematic approach to the evaluation of pigmented nail lesions applies the favored ABCDEF approach to pigmented lesions and is easily remembered and applied.

The most important role for clinicians regarding nail pigmentary lesions is to identify them as early as possible. Full body examinations must always include a viewing of the nails, and any suspicious pigmented lesions must be investigated. A complete personal and family history must be obtained. When in doubt, a biopsy must be done for a histological diagnosis so that treatment can be initiated as quickly as possible. Although a broad list of differential diagnoses exists for the appearance of pigment on the nails, focused questioning and simple investigation can provide a diagnosis and permit rapid progression to treatment.

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