Nail Melanoma In Situ: Clinical, Dermoscopic, Pathologic Clues, and Steps for Minimally Invasive Treatment

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BACKGROUND Nail unit melanoma (NUM) is a variant of acral lentiginous melanoma. The differential diagnosis is wide but an acquired brown streak in the nail of a fair-skinned adult person must be considered a potential melanoma. Dermoscopy helps clinicians to more accurately decide if a nail apparatus biopsy is necessary.

OBJECTIVE Detailed evaluation of clinical and dermoscopy features and description of conservative surgery of in situ NUM.

METHODS Retrospective study of in situ NUM diagnosed and treated with conservative surgical management in the authors' center from 2008 to 2013.

RESULTS Six cases of NUM were identified: 2 male and 4 female patients, age range at diagnosis of 44 to 76 years. All patients underwent complete nail unit removal with at least 6-mm security margins around the anatomic boundaries of the nail. The follow-up varies from 4 to 62 months.

CONCLUSION Nail unit melanomas pose a difficult diagnostic and therapeutic challenge. Wide excision is sufficient, whereas phalanx amputation is unnecessary and associated with significant morbidity for patients with in situ or early invasive melanoma. Full-thickness skin grafting or second-intention healing after total nail unit excision is a simple procedure providing a good functional and cosmetic outcome.

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Nail unit melanoma (NUM), localized either under (subungual) or around (periungual) the nail, is considered a variant of acral lentiginous melanoma that represents approximately 1% to 2.5% of all melanomas in white, 15% to 35% in dark-skinned, and 50% to 58% in Asian individuals.[1–4]

Late diagnosis of ungual melanomas is still a sad reality. This is the reason for the poorer prognosis and lower survival of nail melanoma patients as compared with those with melanomas of other localizations.[5] Despite an obvious brown streak in the nail, both physicians and patients often neglect this important sign for years. Thus, apart from amelanotic nail melanoma, the difficulty of establishing an early diagnosis is not so much the problem that the proximal nail fold and nail plate cover the underlying structures, but a lack of awareness for ungual melanomas. Also, it is often asymptomatic for a prolonged period, and many patients only notice pigmentation after trauma to the area and two thirds seek medical advice very late because of the appearance of the lesion.[6,7]

Longitudinal pigmentation of the nail in light-skinned individuals has a wide range of differential diagnoses, including onychomycosis, drugs, subungual hematoma, nonmelanoma tumors, and striated melanonychia because of functional activation of matrix melanocytes, a lentigo, or a matrix nevus. It is necessary to be aware that an acquired brown streak in the nail of a fair-skinned

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adult person must be considered a potential melanoma.[8] The spread of the pigmentation into the periungual skin (true Hutchinson sign) is indicative of the extension of the disease beyond the nail organ.

Although histopathologic diagnosis remains the gold standard for NUM,[6,9] the clinical diagnosis of longitudinal melanonychia (LM) can be assisted by dermoscopy, which can help clinicians to more accurately decide if a nail apparatus biopsy is required.

Management of melanoma requires consideration of oncologic and reconstructive surgical principles to optimize the chances of cure and quality of life.[10] Nail unit melanomas pose a difficult surgical challenge because of the close relationship between the nail tissues and underlying bone and extensor tendon. Wide excision with phalanx amputation was once considered the first-line therapy[10,11]; however, it is not satisfactory for the patients and has not shown prolongation of disease-free survival, in particular in early cases. The use of tissue-sparing Mohs micrographic surgery for thin melanomas of the nail unit is an alternative that has potential benefit in avoiding amputation. However, it is not available in all centers.[6]

Full-thickness skin grafting after total nail unit excision is a simple procedure that can be performed in cases of NUM in situ. It provides a good cosmetic and excellent functional outcome and does not produce significant donor site morbidity.[1,7,12,13]

Materials and Methods

Six cases of NUM in situ from 2008 to 2013 were retrieved from the dermatopathologic database of the authors' department. Clinical (Figure 1) and dermoscopic (Figure 2) photographs of all cases were examined by 3 dermatologists, and pathology

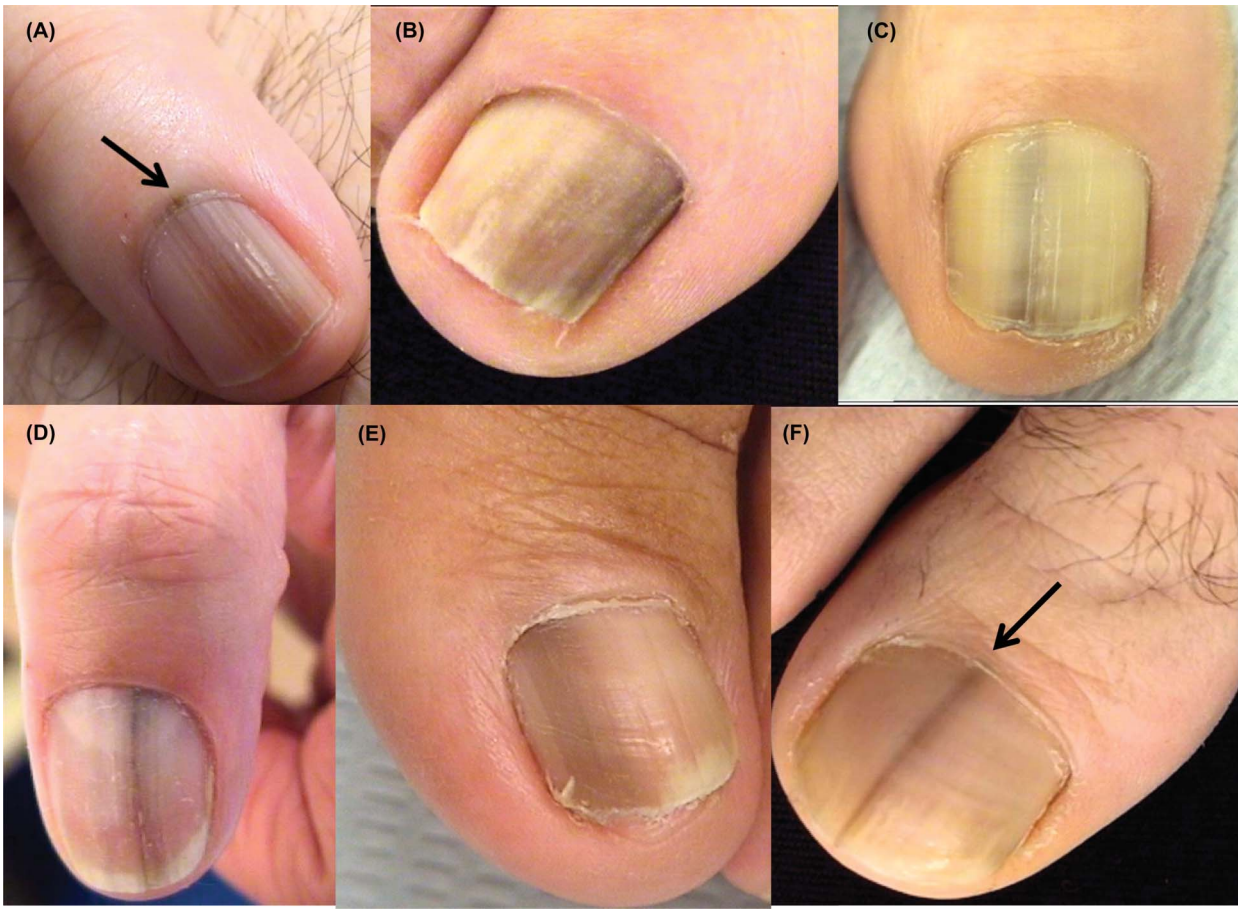

Figure 1. Nail unit melanoma clinical features—LM (A–F) and Hutchinson sign (arrows).

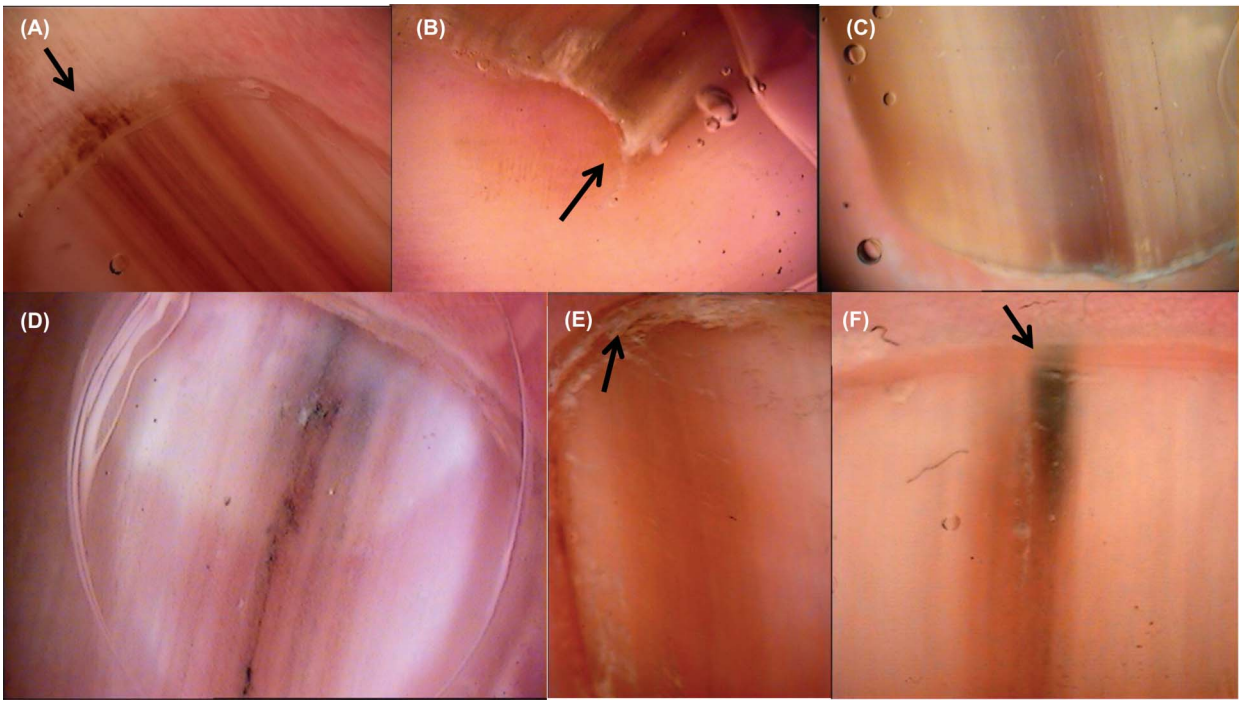

Figure 2. Nail unit melanoma dermoscopic features—brown bands irregular in color, width, and spacing, and Hutchinson sign (arrows). (A–F) Correspond to Figure 1A–F, respectively.

slides (Figure 3) were reviewed by 1 pathologist and 1 dermatopathologist.

Demographic data, including age at the time of diagnosis, sex, localization, family and personal history of melanoma, history of trauma of the affected finger, delay to diagnosis, clinical appearance with presence or absence of periungual pigmentation (Hutchinson sign), dermoscopy features, histopathologic study, treatment modalities, immediate complications of treatment, if any, and follow-up events were recorded (Table 1).

Surgical Management

In all patients, a tangential biopsy specimen was taken from the matrix and nail bed after reflection of the proximal nail fold and separation of the nail plate from the matrix and proximal nail bed (Figure 4). After histopathologic confirmation of in situ nail melanoma, surgical excision of the whole nail unit including the 2 lateral nail folds, the proximal nail fold, and the distal pulp of the finger/toe with an extra margin of 6 mm, was performed. The deep margin was the cortical bone. The excisional defect produced

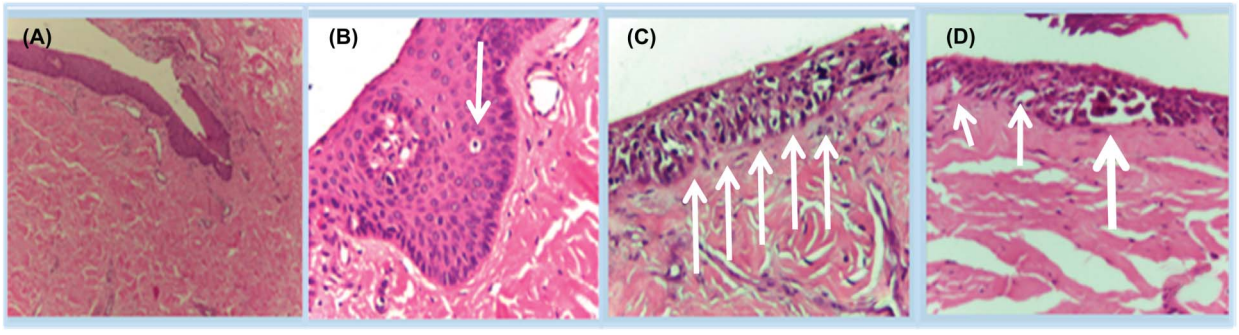

Figure 3. Histopathology of in situ matrix melanomas. Hematoxylin and eosin stain. (A) Almost invisible changes (patient from Figures 1E and 2E). (B) A few cells are obvious (arrow) (patient from Figures 1F and 2F). (C) The entire matrix epitelium shows pagetoid spread of atypical melanocytes (arrows) (patient from Figures 1B and 2B). (D) Lentiginous (small arrows) and nest-like (large arrow) proliferation of atypical melanocytes (patient from Figures 1A and 2A).

TABLE 1. Demographic Data

Features	*Number of Patients (n = 6), n (%)*
Sex	
Male	2 (33.3)
Female	4 (66.7)
Age at diagnosis, years	
Range	44–76
Mean	61
Phototype	
II	3 (50)
III	3 (50)
Location	
Finger	2 (33.3)
Toe	4 (66.7)
Personal history of melanoma	
Yes	1 (16.7)
No	5 (83.3)
Family history of melanoma	
Yes	0 (0)
No	6 (100)
Local trauma history	
Yes	1 (16.7)
Unknown	5 (83.3)
Lesion duration	
Mean	3.5 years
Range	3 months–7 years
<1 years	1 (16.7)
1–3 years	3 (50)
3–5 years	0 (0)
5–10 years	2 (33.3)
Who suspected the lesion	
Patient himself	2 (33.3)
Dermatologist	3 (50)
Family	1 (16.7)

on the dorsal side of the distal phalanx was covered by a full-thickness skin graft taken from the internal aspect of an arm or thigh (depending if the defect was in the finger or toe, respectively), or left for second-intention healing (Figure 5).

Results

Of 6 patients, 4 were women (66.7%) and 2 were men (33.3%). The mean age at the time of diagnosis was 61 years, ranging from 44 to 76 years. All patients were white people, 50% of Phototype II and 50% Phototype III. The demographic features are shown in Table 1.

Two lesions were located on the fingers (1 thumb and 1 fifth finger) and 4 lesions on the toes (all on the hallux). The right side was involved in 4 patients, and the left side in 2 patients.

One patient had a personal history of melanoma in another location, and none gave a family history of melanoma. Only 1 patient reported a previous trauma of the affected nail. The mean delay of diagnosis was 3.5 years, ranging from 3 months to 7 years. The lesion was detected by a dermatologist in 3 cases, by the patient in 2 cases, and by the family in 1 case.

All patients presented an LM. There were no amelanotic cases. The width of the LM was between 3 and 6 mm in 4 patients, narrower than 3 mm in 1, and larger than 6 mm in another one. A clinically apparent Hutchinson sign was present in 2 patients.

The dermoscopic features were suspicious in all cases. All patients had a dark brown background, 5 of them had brown bands with irregular lines in width, spacing, and color. One patient had regular lines. Two cases showed ill-defined edges. Haphazard pigmentation on the hyponychium, called micro-Hutchinson sign, was observed in 4 cases.

A tangential excisional biopsy was performed in all patients. All were diagnosed as in situ melanoma. Clinical, dermoscopic, and pathology features are outlined in Table 2.

Despite clinical suspicion, the pathology may be unclear, that is why 2 patients needed a second biopsy before the diagnosis was reached.

The entire lesion was totally removed in all patients, with safe margins confirmed by histopathology. The entire nail unit was completely removed with an additional margin all around it of at least 6 mm and down to the bone of the terminal phalanx including the periosteum.

The defect was immediately closed in 4 patients with a full-thickness skin graft from the inner arm or the inner thigh, depending on the defect location (finger or toe, respectively). Two patients healed by second intention.

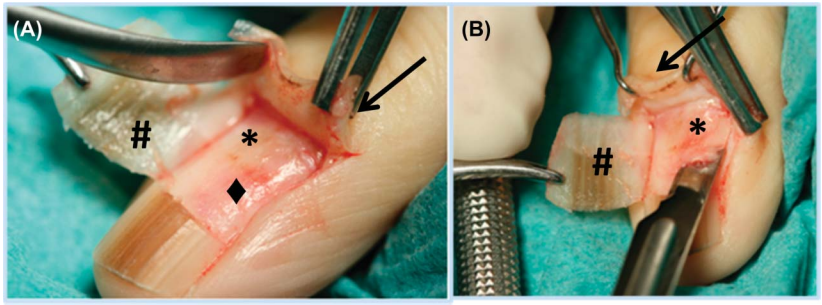

Figure 4. Nail unit melanoma biopsy. (A) Proximal nail fold (arrow) and nail plate (#) elevation. (B) Tangential nail matrix (*) and nail bed (♦) biopsy.

The healing was good in all patients, both cosmetically and functionally (Figure 6). In 2 patients, the defect was left for second-intention healing. Although they had the longest healing period of approximately 2 months, their cosmetic outcome was superior because there was less tissue depression over the surgical defect (Figure 7).

Treatment and follow-up details are given in Table 3. The mean time of follow-up was 25.2 months, ranging from 4 to 62 months. There was no evidence of recurrence or metastases in any of the patients.

Discussion

Nail unit melanomas are frequently more advanced than other melanomas at the time of diagnosis. Consequently, traditional surgical intervention for this type of malignancy has focused predominantly on radical surgery, namely phalanx amputation. Non-amputative excision, described by Haneke and Binder in 1978, is now being advocated in the surgical and particularly the dermatosurgical literature.[6,7,11,14,15]

In the authors' series, there was a female predominance, similar to the literature. This may be related to either genuine gender predominance or to women seeking earlier medical advice. The authors' population was exclusively white, Phototype II or III. Unlike most of the reports, NUM was more frequent on toes than on fingers (4 and 2, respectively). A traumatic etiology suggested as an NUM risk factor was reported by only 1 of the authors' patients, but this remains controversial in the literature.

The authors' series includes only 6 patients, from a small single center, who were diagnosed and treated in a period of 5 years. The latest and largest published

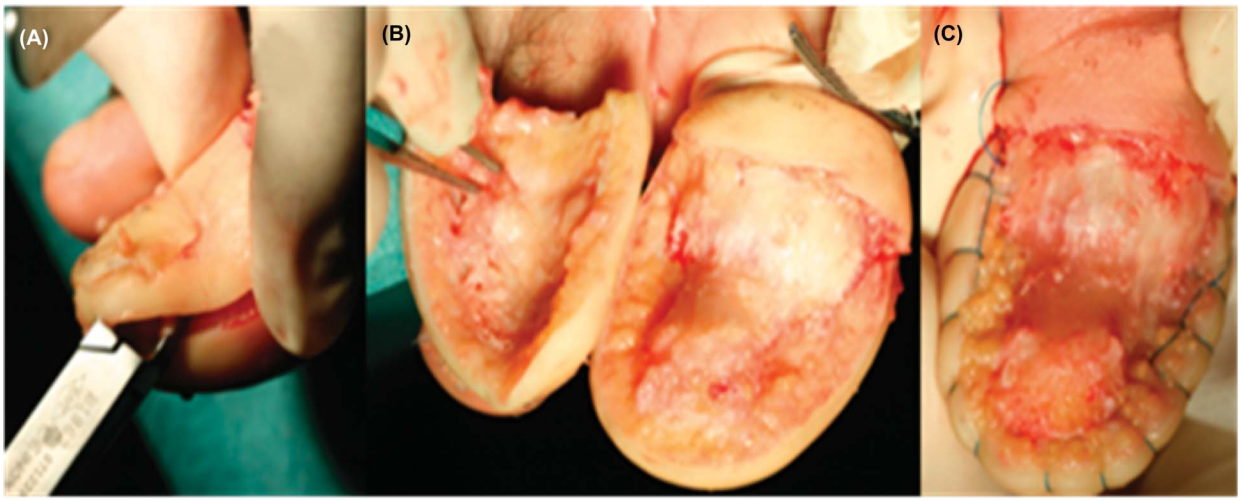

Figure 5. Surgical procedure. (A) An incision is carried around the entire nail organ with a safety margin of 6 mm. (B) The entire nail organ is dissected from the terminal phalanx bone; the undersurface of the surgical specimen is shown. (C) End of surgery; a running locked suture of the wound margin reduces bleeding. This wound is left for second-intention healing.

TABLE 2. Clinical, Dermoscopic, and Pathologic Features

Features	*Number (%) of Patients (n = 6)*
Clinical features	
LM width	
0–3 mm	1 (16.6)
6–6 mm	4 (66.6)
>6 mm	1 (16.6)
Amelanotic lesion	0 (0)
Hutchinson sign	
Yes	2 (33.3)
No	4 (66.6)
Dermoscopic features	
Dark background, brown bands with lines irregular in color	5 (83.3)
Dark background, brown bands with lines regular in color	1 (16.6)
Brown bands with lines irregular in width and spacing	5 (83.3)
Haphazard pigmentation on the hyponychium–Hutchinson sign	4 (66.6)
Ill-defined edges	2 (33.3)
Pathologic features	
Irregular crowding of melanocytes in the basal and suprabasal layers	3 (50)
Confluence of melanocytes, multinucleated cells, and a lichenoid infiltrate	3 (50)
Few melanocytes in the basal and suprabasal layers with irregular distribution. Some hyperchromatic nuclei	1 (16.6)
Occasional melanocyte in high spinous layer	1 (16.6)
Irregular distribution with dense melanocytes in the matrix, hyponychium, and adjacent skin of the tip of the digit but only few cells in the nail bed	3 (50)
Number of biopsies needed until the diagnosis of melanoma in situ	
Mean	1.3
1	4 (66.7)
2	2 (33.3)

series reported 11 patients in 13 years.[15] The incidence of melanoma is increasing every year, although this is not clearly the case for NUM. A population-based study would help to better understand the epidemiology of NUM. Although NUM is rare, given its atypical locations and poor survival rates, it is important that physicians maintain a high index of suspicion in all ethnic groups and closely examine a patient's nail[16] to decrease the often appalling delay in correct diagnosis.

In this series using dermoscopy, two-thirds of the patients had an LM 3 to 6 mm in width and 5 had brown bands with irregular lines in width, spacing, and color. Surprisingly, 1 patient had regular lines in color. A clinically apparent Hutchinson sign was present only in 2 patients, but a haphazard pigmentation on the hyponychium, called micro-Hutchinson sign, was observed in 4 cases, underlining the importance of dermoscopy.

The delay of diagnosis averaged 3.5 years, ranging from 3 months to 7 years, less than the 5 years of the largest series of in situ melanomas published. This may also reflect that the authors' policy to biopsy all acquired LMs in adults. In contrast, the most recent series of 124 NUMs of all levels claimed a delay of 2.2 years.[17]

In this series, the lesion was detected during a routine check for pigmented lesions in 3 cases, by the patient in 2 cases and by the patient's family in 1 case.

Clinical suspicion and close inspection are most important to recognize early NUM. A persistent search, sometimes culminating in several biopsies, is needed until an accurate diagnosis is made.[18,19] The presence of a brown pigmentation wider than 5 mm and overlaid by longitudinal lines irregular in their thickness, spacing, color, or parallelism is highly suspicious for a melanoma. On Table 4, the main differences between early NUM and advanced clear-cut NUM are outlined.

The etiology, pathogenesis, and natural history of NUMs remain poorly understood. Although most patients do not recall a previous trauma, the majority of NUM lesions are on the thumb and hallux that are typically locations of minor chronic or repeated trauma. Thus, the authors cannot exclude a role of recurrent trauma on melanoma development.[20,21] One patient only could remember a previous trauma to the affected nail unit.

Unlike cutaneous melanoma, UV exposure does not seem to play a relevant role in NUM because the nail plate is too dense for significant light penetration.[2,22]

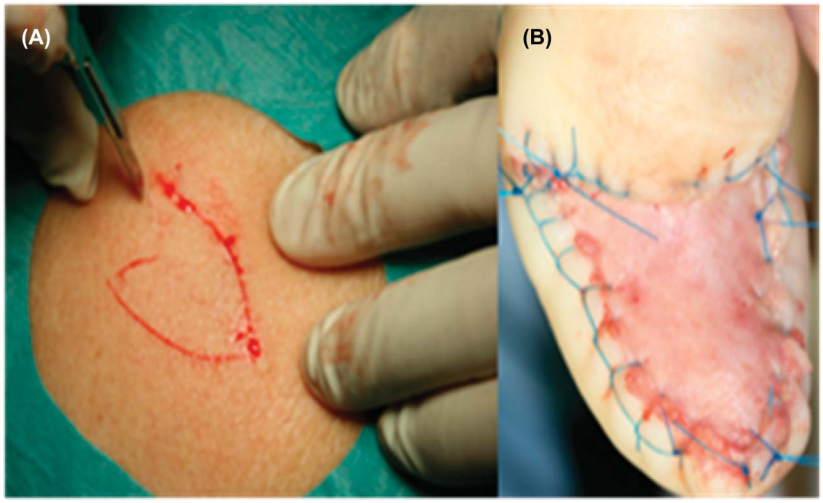

Figure 6. Grafting of the defect. (A) Full-thickness skin graft designed on an inner thigh. (B) The graft is sutured into place with a running locked suture.

Dermoscopic examination of the free edge of the nail plate gives information on the lesion location: pigmentation of the dorsum of the nail plate is in favor of a proximal nail matrix lesion, whereas pigment in the lower part of the nail edge indicates a lesion of the distal matrix.[23] The International Study Group on Melanonychia stated that in the adult, a brown background associated with longitudinal lines that are irregular in color, width, spacing, and parallelism is suggestive of malignant melanoma. Also an individual line that shows irregularity in color or width along its length and a dark background with the areas of different hues of pigmentation even in the absence of irregular lines, are considered suspicious of melanoma.[19] Widening of the band proximally stands for enlargement of the width of the lesion.[2] Although dermoscopy can help, particularly in micro-Hutchinson and slightly irregular melanonychias, the problem with dermoscopy is that in melanonychia it only gives a unidimensional picture of the result of a melanocytic lesion in the matrix in contrast to dermoscopy of the skin, which gives a bi-dimensional picture of the lesion itself. Thus, dermoscopy may often help but can be misleading as shown by 1 of the authors' cases.

Direct dermoscopic examination of the nail bed and matrix enables the visualization of pigmentation directly in its original site, revealing aspects not observed when the nail plate is interposed between the pigmented lesion and the dermoscope.[24] This provides information that can help the surgeon to determine whether the lesion should be excised or can simply be submitted for biopsy, which is especially important in the case of large bands that cannot be excised without subsequent nail scarring. However, intraoperative nail matrix dermoscopy, performed directly on the matrix after nail plate avulsion, is an invasive procedure that cannot routinely be performed in all centers.[25]

Recently, an intraoperative ex vivo diagnosis by reflectance confocal laser microscopy has been described. It is an expensive technique used in investigation and not available for the majority of centers, but this type of examination of the nail matrix is an efficient diagnostic approach of LM that is believed to permit an extemporaneous diagnosis of malignancy and a 1-step surgical treatment of in situ or minimally invasive melanoma, dramatically reducing the duration of postoperative disability.[26]

Histopathology of clinically typical nail melanoma is usually unequivocal[2]; however, very early cases may pose extreme difficulties. Amin and colleagues[27] proposed the melanocyte number per 1 mm stretch of the dermo-epithelial junction as a means to distinguish between melanomas and benign melanocytic lesions. Some authors stress that there is a lymphocytic infiltrate associated with ungual melanoma, but the authors have not seen this in any of the authors'

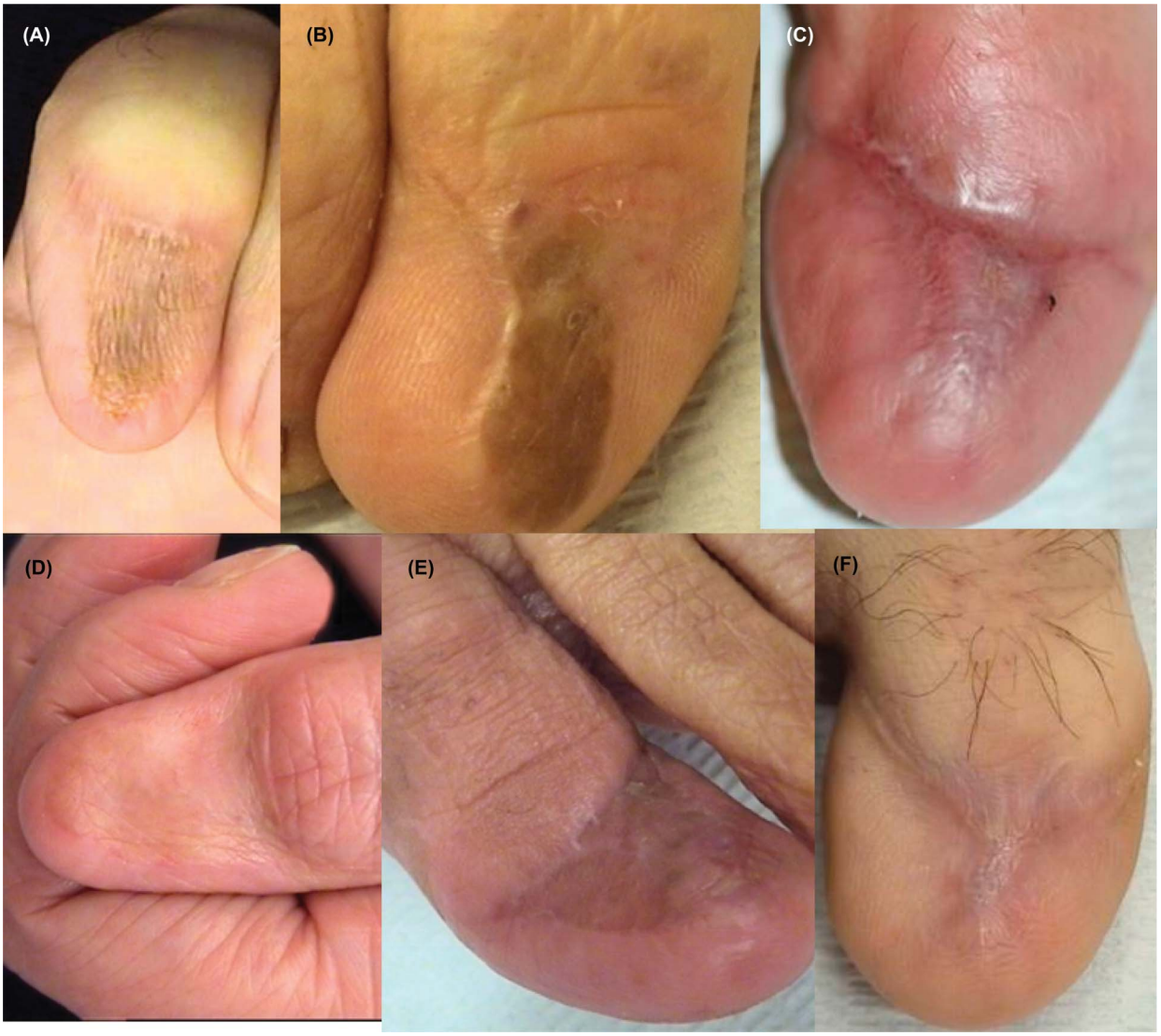

Figure 7. Nail unit melanoma after surgical outcome—good aesthetic and functional outcome. (A) Corresponds to the same patient as in Figures 1A and 2A, (B) corresponds to Figures 1B and 2B, (C) corresponds to Figures 1C and 2C, (D) corresponds to Figures 1D and 2D, (E) corresponds to Figures 1E and 2E, and (F) corresponds to Figures 1F and 2F. (C and F) Were allowed to heal secondarily.

cases. Intraungual melanocytes as a sign of pagetoid spread are seen in roughly one third of the cases and are strong evidence for a melanoma. Further, the shape of the melanocyte dendrites is plumper in melanomas.[28] Occasionally, hardly any melanocyte is detected despite an acquired wide brown band in an elderly person. Nevertheless, this clinical scenario is particularly suspicious, with a high risk of nail melanoma despite lack of obvious morphologic features histologically.[28,29] The number of atypical melanocytes and the severity of atypia seem to be correlated with the overall number of melanocytes in the matrix.

In a person of color, whether black or Asian, longitudinal brown striation is more and more frequent with age.[4,16,30] The melanonychias range from single light brown bands to almost entirely black nails. Most of these discolorations are due to melanocyte activation, which is said to yield rather a grayish color than brown.[19] However, this may be extremely difficult to differentiate, and it has therefore been proposed to look for the "ugly duckling sign," which means that in dark-skinned individuals with many pigmented nails, one should look for a particularly black streak that stands out from the rest of the

TABLE 3. Treatment and follow-up

Features	*Number (%) of Patients (n = 6)*
Treatment	
Excisional biopsy	6 (100)
Total nail unit excision, until the phalanx and immediately full-thickness skin grafting	4 (66.7)
Total nail unit excision, until the phalanx and second-intention healing	2 (33.3)
Follow-up	
Recurrence	
Yes	0 (0)
No	6 (100)
Metastasis	
Yes	0 (0)
No	6 (100)
Follow-up time, months	
Mean	25.2
Range	4–62

brown bands.[31] Any nail dystrophy in conjunction with a melanonychia is suspicious for ungual melanoma unless otherwise proven.

The follow-up of this series is short, mean time was 25.2 months, ranging from 4 to 62 months. Longer-term data, of at least 5 years, are necessary for stronger conclusions.

Conclusion

A high index of suspicion is mandatory to diagnose NUM. A biopsy is recommended for suspicious LM acquired after puberty in fair-skinned individuals or in the presence of LM showing rapid and progressive growth.[12] The use of noninvasive techniques such as dermoscopy is valuable for the better selection of cases, in which a pathologic examination is indicated.[32]

Because dermoscopy gives finer details, it can be of help to identify slightly irregular melanonychias and micro-Hutchinson, which would not be seen otherwise by the naked eye. However, nail dermoscopy does not allow the melanocytic lesion to be observed directly; this is only possible with intraoperative direct matrix dermoscopy.

TABLE 4. Nail Unit Melanoma Clinical, Dermoscopic, and Pathology Features, Early Versus Late Changes

	Early NUM	*Late NUM*
Clinical features[2]		
	Narrow LM (<5 mm)	Large, LM rapidly changing (>5 mm)
	Brown discoloration	Black discoloration
	Discrete nail defect	Nail dystrophy
	Discrete Hutchinson sign	Evident Hutchinson sign
		Oozing or bleeding lesion
		Nodular lesion
Dermoscopic features[19]		
	Dark background	Black background
	Brown bands with lines irregular in width and/or spacing and/or color	Structureless pattern
	Discrete Hutchinson sign	Evident Hutchinson sign
	Ill-defined edges	
Pathology features[2]		
	Irregular crowding of melanocytes, mostly in the basal and suprabasal layers	Dense aggregations of melanocytes (39–136 melanocytes/mm basal layer) with large and atypical nuclei, often long dendrites, and pagetoid spread of cells to the upper layers of the matrix epithelium and into the nail plate
	Confluence of melanocytes, multinucleated cells, and a lichenoid infiltrate even when only focal, are in favor of a melanoma	

The clinical diagnosis should be supported by tools such as dermoscopy, which may contribute to the decision if the lesions need biopsy. Only an early diagnosis can achieve a better outcome.

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