

Nail Apparatus Melanoma: Experience of 10 Years in a Single Institution

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Keywords

Nail apparatus melanoma · Melanonychia · Ungual melanoma · Hutchinson's sign · Nail melanoma epidemiology

Abstract

Background: Nail apparatus melanoma (NAM) is rare. The higher mortality reported in the literature is most likely due to advanced disease associated with delayed diagnosis and treatment. **Objective:** All patients diagnosed with NAM were followed at a single reference center during a period of 10 years, with emphasis on dermatological and histological findings. Clinical outcomes were included. **Methods:** A retrospective review of medical records, photographs, and histopathological examination. **Results:** 73.7% of the patients were female and their mean age was 47 years. Caucasian and African-American patients had a similar incidence (47.4%). There was only 1 Asian patient in this study (5.3%). All patients presented with nail plate pigmentation. The mean prediagnosis duration was 33 months. A total of 63.2% patients had in situ melanoma and an average Breslow index of 2.18 mm in invasive cases. Fifteen patients underwent conservative surgery and 3 underwent phalanx amputation. All patients survived, and 4 have had more than a 5-year follow-up. **Conclusion:** In situ lesions showed longitudinal bands or total melanonychia with no nail dystrophy. Invasive cases presented with dystrophic lesions (longitudinal split-

ting of the nail). Conservative surgery provides a good option without worsening the prognosis. All dermatologists should be aware of early signs of NAM, since prognosis depends on early treatment.

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Introduction

Nail apparatus melanoma (NAM) can be either subungual or periungual, depending on whether it is located under the nail or around the nail, and most arise from abnormal nail matrix melanocytes [1, 2]. It was first described by Boyer [3] in 1834 and then by Hutchinson [4] in 1886. NAM is considered as a subgroup of acral lentiginous melanomas, comprising only 0.7–3.5% of all forms of melanoma [5–7].

Initial clinical manifestations comprise a longitudinal melanonychia that may progressively enlarge and involve the whole plate. Periungual pigmentation (Hutchinson's sign) may be present. More advanced cases may show partial or complete nail plate destruction [8]. The presence of multiple shades of brown and black, homogenous black pigmentation, melanonychia with width of 3 mm or more or an irregular or blurred border must raise suspicion for melanoma [9, 10].

Despite being rare, NAM accounts for a disproportionately higher mortality when compared with melano-

Table 1. Nail apparatus melanoma clinical features

Sex, <i>n</i> (%)	
Male	5/19 (26.3)
Female	14/19
Age, years	
Range	8–80
Mean	47
Ethnicity, <i>n</i> (%)	
Caucasian	9/19 (47.4)
African-American	9/19 (47.4)
Asian	1/19 (5.3)
Lesion site, <i>n</i> (%)	
Fingernail	12/19 (63.2)
Toenail	7/19 (36.8)
Left side	8/19 (42.1)
Right side	11/19 (57.9)
First fingernail	9/19 (47.4)
First toenail	5/19 (26.3)
Second fingernail	1/19 (5.3)
Second toenail	1/19 (5.3)
Fourth fingernail	1/19 (5.3)
Fifth fingernail	2/19 (10.5)
Fifth toenail	1/19 (5.3)
Clinical manifestations at initial diagnosis, <i>n</i> (%)	
Nail dystrophy	8/19 (42.1)
Periungual pigmentation	9/19 (47.4)
Eponychium	5/19 (26.3)
Lateral nail fold	5/19 (26.3)
Hyponychium	5/19 (26.3)
Total nail pigmentation	8/19 (42.1)
Partial nail pigmentation	11/19 (57.9)
Nail bed mass	2/19 (10.5)
Amelanotic lesion	0/19 (0.0)
Prediagnosis duration, months	
Range	3–120
Mean	33
Extracutaneous involvement at diagnosis, <i>n</i> (%)	
Lymph node involvement	3/19 (15.8)
Visceral involvement	0/19 (0.00)
AJCC stage at diagnosis, <i>n</i> (%)	
0	12/19 (63.2)
I	2/19 (10.5)
II	2/19 (10.5)
III	3/19 (15.8)
IV	0/19 (0.00)
History, <i>n</i> (%)	
Family	0/19 (0.00)
Personal	1/19 (5.3)

ma elsewhere, with a 5-year survival rate of about 55% [11]. Clinicopathological features affecting an NAM prognosis are: age at diagnosis, number of dermal mitoses, Breslow thickness, ulceration, amelanosis, and vascular invasion [8, 12, 13]. Tan et al. [14] suggest that a higher American Joint Committee on Cancer (AJCC) stage is

Table 2. Comparison of histopathological features

Thickness, <i>n</i> (%)	
≤1 mm	14/19 (73.7)
>1 to ≤2 mm	1/19 (5.3)
>2 to ≤3 mm	3/19 (15.8)
>3 to ≤4 mm	0/19 (0.0)
>4 (T4) mm	1/19 (5.3)
In situ melanoma, <i>n</i> (%)	12/19 (63.2)
Ulceration, <i>n</i> (%)	3/19 (15.8)
High mitotic rate >5/mm ² , <i>n</i> (%)	2/19 (10.5)
Vertical growth phase, <i>n</i> (%)	7/19 (36.8)
Regression, <i>n</i> (%)	0/19 (0.0)

the only significant predictor of a lower survival. Early excision is the only treatment known to increase survival thus far [12, 14]. Diagnosis plays a crucial role and dermatologists should be aware of early signs of NAM.

In this study, we report all patients diagnosed with NAM who were followed at a single reference center during a period of 10 years, with emphasis on dermatological and histological findings and clinical outcomes.

Methods

A search was conducted in our database for cases in which the diagnosis of NAM was suspected between August 2007 and February 2017. The inclusion criterion was a diagnosis of melanoma in the nail apparatus confirmed by histopathology and immunohistochemistry results. All biopsy slides were reviewed. NAM was defined as a melanoma arising in the nail bed, nail matrix, or periungual tissue.

A retrospective review of all patients' medical records, photographs, and histopathological examination was performed to analyze the following data: sex, age at diagnosis, ethnicity, lesion site, initial clinical manifestation, family or personal history of previous melanoma, prediagnosis duration, treatment, and patient survival. The following histopathological characteristics were reviewed: subtype, Breslow thickness, ulceration, mitotic rate, regression, and vertical growth phase. The disease stage was determined according to the AJCC classification.

Data were collected retrospectively from medical records. Patients did not undergo further examination or additional procedures or appointments, aside from the usual visits.

Results

A retrospective review of the Hospital das Clinicas via the São Paulo database identified 19 patients diagnosed with NAM who were treated between August 2007 and February 2017. All data are available in Tables 1 and 2 and Figures 1–5.

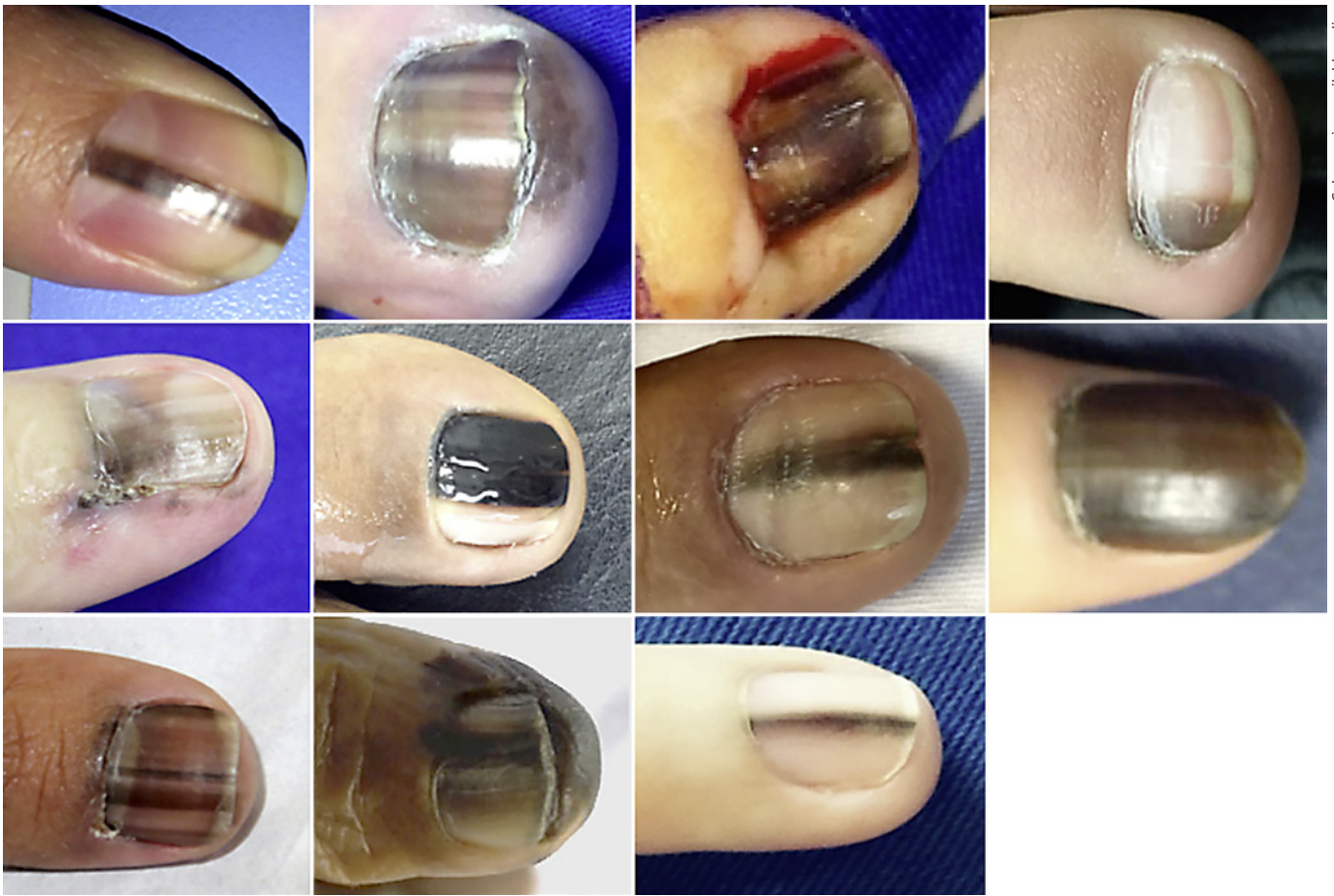


Fig. 1. Stage 0 – in situ melanoma.

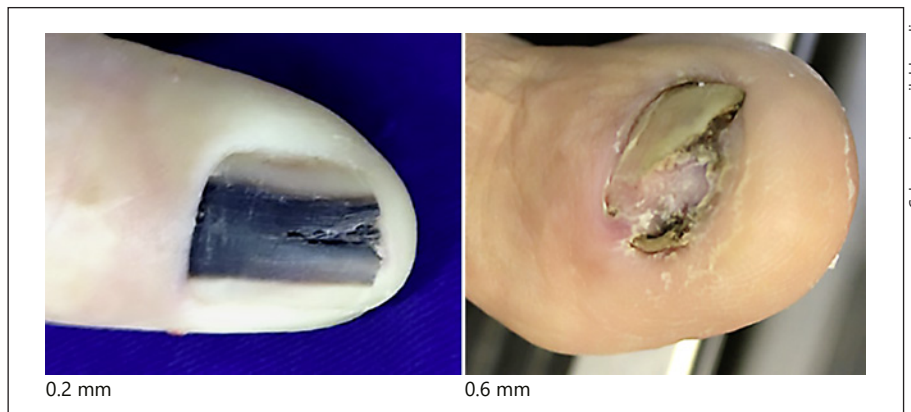


Fig. 2. Stage I.

There were 5 male and 14 female patients, with age ranging from 8 to 80 years (mean age 47 years). Nine patients were Caucasian, 9 African-American, and 1 was Asian. Twelve had fingernail involvement and 7 had toenail involvement. The right side was more prevalent than

the left side (11:8). The first fingernail was the most prevalent (9 patients) and the first toenail was the second most prevalent (5 cases).

NAM clinical manifestations vary. Partial to total nail pigmentation and periungual pigmentation were ob-

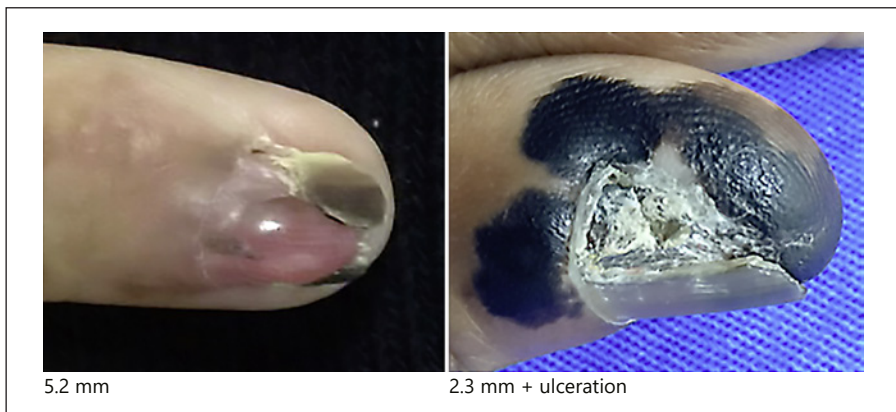


Fig. 3. Stage II.

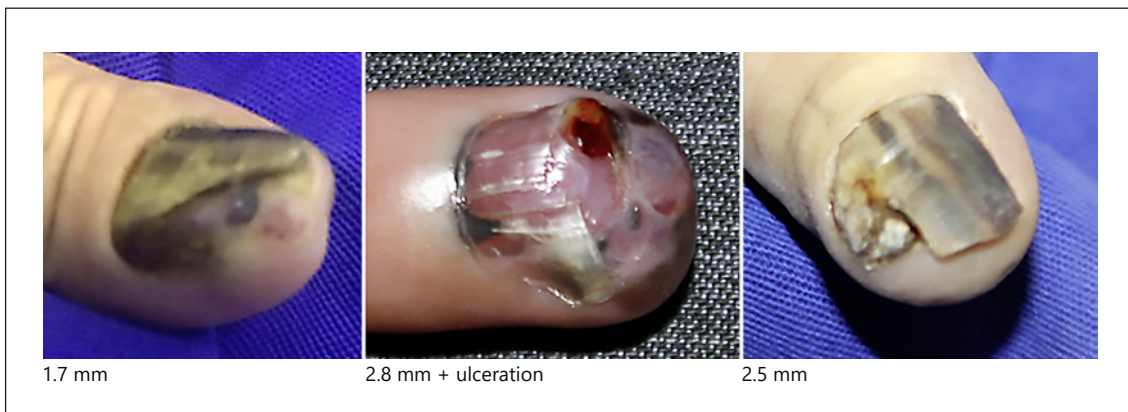


Fig. 4. Stage III.

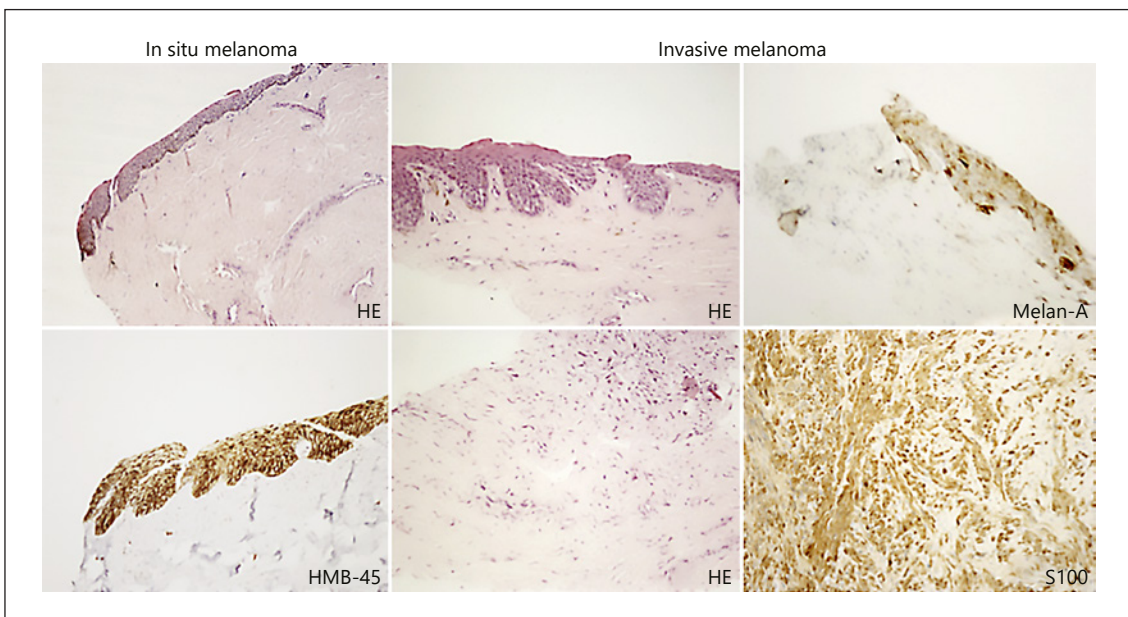


Fig. 5. In situ melanoma versus invasive melanoma.

served in in situ cases. Invasive NAM presented nail pigmentation, nail dystrophy, and 1 had nail bed mass.

The mean prognosis duration was 33 months (3–120 months). There was 1 patient with a history of cutaneous melanoma in our series.

There were 12 in situ melanomas, 2 with a thickness >1 mm, 1 between 1 and 2 mm, 3 between 2 and 3 mm, and 1 with more than 4 mm. Three cases had histological ulceration and 2 cases presented a high mitotic rate. A vertical growth phase was observed in 7 patients, but regression was not observed. There were 3 cases with lymph node involvement.

On the left side of Figure 5, an in situ melanoma with atypical melanocytes ascension is shown. On the right side, an invasive melanoma with melanocytes with nuclear retraction with pigmentary effusion in the superficial dermis is shown. Analyzing the underlying dermis, a fusocellular proliferation was observed. Melan-A marked melanocytes in the epithelium of the matrix, but not in the dermis. Only S100 highlighted positivity of the fusocellular component of the dermis.

Discussion

There are still few studies on NAM. In the 10 years of this study, only 19 patients were diagnosed with NAM in our Dermatology Center, where 20,000 [15] new patients are seen every year.

In our series, there was a threefold female predominance. The literature is unclear about which gender is more affected [1]. In Japan, Korea, and Taiwan, there is a male predominance [16–18], whereas a female predominance is observed in Western countries [6, 19, 20].

The patients had a mean age of 47 years, which is younger than in the literature (53–66 years) [18, 21–23]. NAM is more frequent between the ages of 50 and 70 years [1], but in rare occasions can also be observed in children [24, 25]. More than half of the subjects were younger than 50 years, including an 8-year-old child.

As for ethnicity, Caucasian and African-American patients had a similar incidence (47.4%). There was only 1 Asian patient in this study (5.3%). In absolute numbers, NAM incidence in Caucasians and African-Americans is very similar [11, 26], although NAM represents 20% of all melanoma cases in African-Americans and 1.5–2% of all melanoma cases in Caucasians [1, 21, 26, 27].

In our study, a significant amount of time passed from the perception of the lesion by the patient to the diagnosis, with a mean duration of 33 months (range 3–120).

Nevertheless, it is a shorter period of time compared to 61 and 55 months in the studies conducted by Lee et al. [18] and High et al. [21], respectively. NAM is often only diagnosed many years or even decades after the initial clinical manifestations. A long prediagnosis duration can contribute to a poor prognosis, as reported in the literature.

Most of the studied lesions were located on the first fingernail (47.4%) and first toenail (26.3%). In the literature, the first fingernail is also the most affected digit, followed by the first toenail [1]. Fingernail involvement was three times more frequent than toenails, as seen in previous studies [20, 22, 28]. Whether trauma plays an important role is not clear, but 47.4% of patients of this study reported a history of trauma preceding NAM [28, 29].

All patients showed some degree of melanonychia, and 42.1% had total nail pigmentation. Hutchinson's sign was observed in 47.4%, of which 26.3% were on the proximal nail fold, 26.3% on the lateral nail fold, and 26.3% on the hyponychium. Nail dystrophy was observed in 42.1% and nail bed mass in 10.5% patients. There were no cases of amelanotic lesions in this study.

In this series, we observed that in situ lesions showed longitudinal bands or total melanonychia, but no nail dystrophy. All invasive cases presented with some degree of dystrophy, at least a minimum of longitudinal nail splitting.

No patients had a familiar history of melanoma, and only 1 patient had a history of skin melanoma. At diagnosis, 15.8% had lymph node involvement and no visceral involvement was observed. The AJCC stage [30] proportion at diagnosis was 63.2% in stage 0, 10.5% in stage I, 10.5% in stage II, 15.8% in stage III, and 0 in stage IV.

NAM histologic criterion is still under discussion. The presence of melanocytes in the suprabasal position is physiological in the matrix within the lower 2–4 germinative cell layers. Histological examination of nail melanoma biopsy can be difficult, and immunohistochemical investigations are often helpful [31]. Histologic examination revealed a predominance of in situ melanoma (63.2%). In situ melanoma is characterized by an increased number of melanocytes in the basal cell layer and single melanocytes predominate over the nest in most fields. Nuclear atypia (nuclear enlargement, angular and hyperchromatic nuclei, and prominent nucleolus) are present as a pagetoid spreading. Invasive melanoma is characterized by atypical melanocytes also invading the dermis, which usually starts in the nail bed [32, 33]. The average depth of invasive cases was 2.18 mm, in contrast

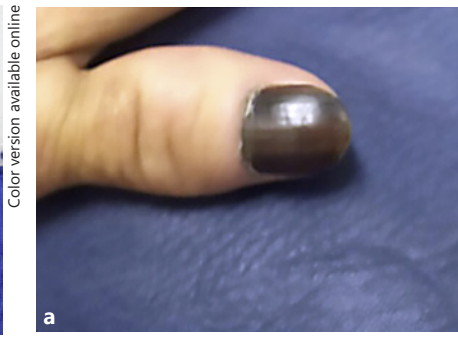


Fig. 6. Conservative surgery of in situ nail apparatus melanoma.

Fig. 7. Conservative surgery. **a** Preoperative. **b** Postoperative.

to 4.80 mm in the study by Banfield et al. [34] including 105 patients.

Melanocytes can be better observed via immunohistochemical stains, including S100, HMB-45, Melan-A, and MiTF. The HMB-45 was the most intense marker in most cases. The sensitivity of the S100 protein was high in the dermal component of the invasive melanoma, whereas its intraepidermal component was weak or negative for this marker.

Traditional first-line therapy for NAM used to be phalanx amputation [35, 36]. More recently, a conservative nonamputative treatment method has been considered in cases of minimally invasive NAM or in situ NAM [37]. It consists of a wide excision of the whole nail apparatus with safety margins [1, 35, 36, 38]. In this study, only 3 patients with a more advanced disease underwent phalanx amputation, whereas the 15 others underwent conservative surgery (Fig. 6, 7), and 1 is still under treatment with a surgical approach scheduled.

All 19 patients survived, of which 4 were diagnosed more than 5 years prior. Fifteen patients were diagnosed in the last 5 years and are still being followed. All are without signs of recurrence. Nevertheless, NAM is often related with a poor prognosis. The reported 5-year survival rates vary between 16 and 76% [6, 12, 20, 39–42].

Conclusion

Due to its rarity, there are still few studies that have examined NAM. The literature is still unclear as to whether a poor prognosis associated with NAM is due to an intrinsic aggressiveness of the tumor or a delay in diagnosis. In this study, an earlier diagnosis was made, since most cases were in situ NAM, and achieved a better outcome

than the rates described in the literature. This reinforces the notion that early treatment is crucial for prognosis. In situ lesions showed longitudinal bands or total melanonychia but no nail dystrophy, whereas all invasive cases presented with some degree of dystrophy, at least with a minimum of longitudinal nail splitting. Conservative surgery was performed for all in situ melanoma patients and did not worsen the prognosis with much less morbidity. In conclusion, physicians and dermatologists, in particular, should be aware of the early signs of NAM, since the prognosis depends on early treatment. Although more studies need to be performed, we hope to have improved the knowledge regarding NAM.

Statement of Ethics

All patients signed an informed consent allowing the publication of this information.

Disclosure Statement

The authors have no conflict of interest to disclose. There was no financial sponsorship.

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