

# Morphological features of naevoid melanoma: results of a multicentre study of the International Dermoscopy Society

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## Summary

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### Accepted for publication

3 November 2014

### Funding sources

Melanoma Unit, Hospital Clinic de Barcelona, Institut d'Investigacions Biomèdiques August Pii Sunyer IDIBAPS, Universitat de Barcelona, Barcelona, Spain; and Centro de Investigación Biomédica en Red de Enfermedades Raras (CIBERER), ISCIII, Barcelona, Spain.

### Conflicts of interest

None declared.

**Background** Naevoid melanoma (NeM), a rare variant of melanoma, can be difficult to detect as its clinical and histopathological morphology can simulate a naevus. **Objectives** To describe the clinical and dermoscopic features associated with NeM. **Methods** Lesions with a histopathological diagnosis of NeM were collected via an e-mail request sent to all members of the International Dermoscopy Society. All lesions were histopathologically reviewed and only lesions fulfilling a set of predefined histopathological criteria were included in the study and analysed for their clinical and dermoscopic features. **Results** Twenty-seven of 58 cases (47%) fulfilled the predefined histopathological criteria for NeM and were included in the study. Clinically, 16 of the 27 NeMs presented as a nodular lesion (59%), eight (30%) as plaque type and three (11%) as papular. Analysis of the global dermoscopic pattern identified three types of NeM. The first were naevus-like tumours ( $n = 13$ , 48%), typified by a papillomatous surface resembling a dermal naevus. In these lesions local dermoscopic features included irregular dots/globules (46%), multiple milium-like cysts (38%) and atypical vascular structures (46%). The second type were amelanotic tumours ( $n = 8$ , 30%), typified by an atypical vascular pattern (75%). The third type consisted of tumours displaying a multicomponent pattern ( $n = 4$ , 15%), characterized by classical local melanoma-specific criteria. Two lesions (7%) were classified as mixed-pattern tumours as they did not manifest any of the aforementioned patterns. **Conclusions** While NeMs may be clinically difficult to differentiate from naevi, any papillomatous lesion displaying dermoscopically atypical vessels and/or irregular dots/globules should prompt consideration for the possible diagnosis of NeM.

### What's already known about this topic?

- Naevoid melanoma is a rare variant of melanoma, and can be difficult to detect as its clinical and histopathological morphology can simulate a naevus.

### What does this study add?

- This study provides new insights into the clinical and dermoscopic morphology of naevoid melanoma, facilitating its clinical recognition.

The entity called naevoid melanoma (NeM) refers to a rare, diagnostically deceptive variant of melanoma that can mimic a naevus both clinically and histopathologically.<sup>1–11</sup> The normal-appearing architectural structure and the bland cytological features can resemble those of a dermal naevus, leading to misdiagnosis, with eventual recognition of the true nature of the lesion after it has metastasized or recurred. Diagnostic pathological clues can be found on careful inspection of the lesion at higher magnification, permitting the recognition of unusual cytological features and mitotic figures, especially in the deeper portion of the lesion.<sup>3–5</sup>

The clinical features of NeM are described as dome-shaped or verrucous, variably pigmented lesions arising on the trunk or limbs of adult patients.<sup>1–19</sup> While dermoscopy has been proven to improve the recognition of various pigmented and nonpigmented skin tumours,<sup>20,21</sup> including various subtypes of melanoma,<sup>22–27</sup> no data exist on the dermoscopic pattern of NeM. The aim of this multicentre study was to describe the dermoscopic features most frequently associated with NeM.

## Materials and methods

Lesions with a histopathological diagnosis of NeM were collected from January 2013 to December 2013 via an e-mail request sent to all members of the International Dermoscopy Society. For each lesion, a patient data intake form (including sex, age, personal and family history of melanoma, total number of naevi, histopathological information, and lesion anatomical location), high-resolution clinical and dermoscopic images, and histopathological slides (or representative digital images of the histology) were collected. All data and digital images were assigned a unique identifier, then anonymized and sent via e-mail to the study coordinator (C.L.).

Before case inclusion, three dermatopathologists reviewed the histopathology of all cases, and only lesions diagnosed as NeM by consensus agreement were included. The cases were classified according to predefined histopathological criteria previously published in the literature<sup>1–10</sup> and in standard textbooks.<sup>12–19</sup> Among the several reported criteria, the following were considered essential by the three pathologists: (i) bland cytological appearance of melanocytes, (ii) apparent maturation in the deep dermis, (iii) absence of epidermotropism and

(iv) rapid mitotic activity.<sup>4–9</sup> Only lesions fulfilling all of these criteria were included in the study, and were further classified according to the architectural growth pattern (nodular/verrucous or plaque type). Some of the melanomas were considered separately as 'predominantly naevoid' when they included a minor component (< 10% of the entire lesion) consisting of a pattern other than NeM.

After histopathological re-evaluation, cases diagnosed as NeM were included in the study and subsequently analysed for their clinical and dermoscopic features. Lesions were first evaluated for their primary clinical morphological characteristics (macule, papule, plaque, nodule) and colour (skin coloured, pink, red, blue, white, brown, black). All digital images were then reviewed by two expert dermoscopists (C.L. and G.A.) and each lesion was scored according to the global pattern as previously reported.<sup>22</sup> Local dermoscopic features included the presence of the following elements:<sup>22,28,29</sup> comedo-like openings, milia-like cysts (more than three), blue-grey ovoid structures, arborizing vessels, hairpin vessels, glomerular vessels, dotted vessels, linear irregular vessels, comma vessels, red lacunae, atypical network, blue-white veil, irregular streaks, regression, irregular pigmentation, irregular dots/globules, and atypical vascular pattern (polymorphous vessels corresponding to any combination of two or more different types of vascular structures).<sup>28,29</sup>

Institutional review board approval for this study was waived.

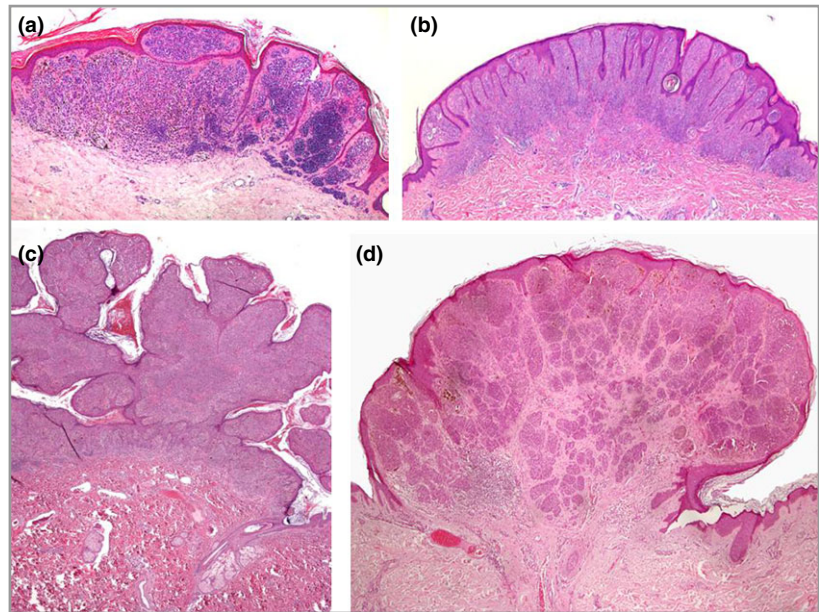
## Results

### Study population

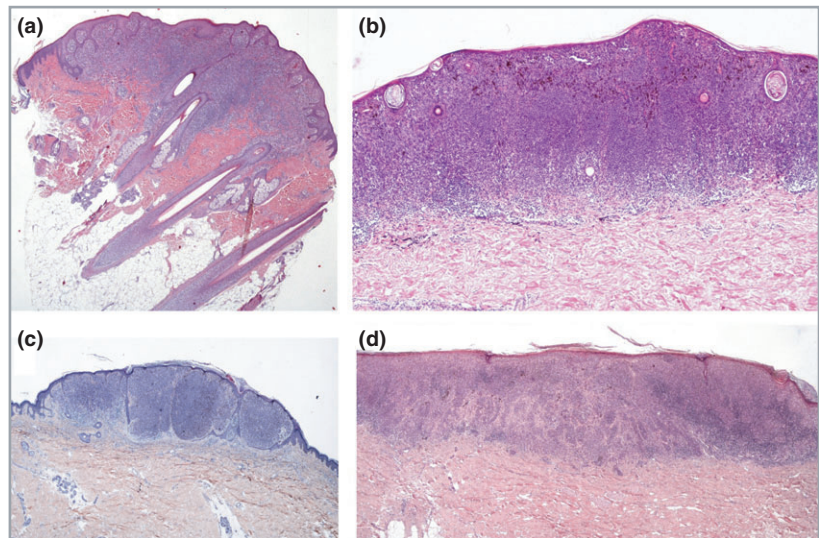
In total 58 lesions were collected. For 46 lesions the original histopathological section slides stained with haematoxylin and eosin were obtained for evaluation, and in 12 cases only digital, high-resolution histopathological images were available. Twenty-seven cases (47%) fulfilled the predefined histopathological criteria for NeM and were included in the final study.

Nineteen (70%) of the 27 lesions showed a nodular or verrucous topography, whereas eight (30%) had plaque-type architecture (Figs 1 and 2). Twenty three lesions (85%) were

**Fig 1.** Naevoid melanoma with a nodular, partially papillomatous architecture. (a) A scanning view of a nodular naevoid melanoma with a symmetrical silhouette and deceptively benign epidermal hyperplasia. (b) The verrucous pattern of growth of this melanoma resembles a benign papillomatous naevus. (c) Low magnification of a nodular naevoid melanoma with a polypoid architecture. (d) Overview of a naevoid melanoma with symmetrical architecture resembling a dermal naevus. Haematoxylin and eosin-stained sections, original magnification  $\times 20$ .



**Fig 2.** Naevoid melanomas with a plaque-type silhouette. (a) Low-power view of a plaque-type naevoid melanoma showing deep perifollicular invasion of the dermis. (b) An asymmetrical, heavily pigmented papule of naevoid melanoma. (c) A scanning view of a well-circumscribed, slightly asymmetric, plaque-type naevoid melanoma. (d) A rather flat naevoid melanoma with an irregular dermal contour. Haematoxylin and eosin-stained sections, original magnification  $\times 20$ .



classified as pure NeM and four (15%) were considered predominantly NeM. Among the latter, three lesions had a focal superficial spreading component, and one lesion had some peripheral nests consisting of large spitzoid melanocytes.

Eleven of the patients were female (41%) and 16 were male (59%), with a mean age of 51.5 years. Twelve tumours were located on the trunk (44%), seven on the upper extremities (26%), five on the lower extremities (19%) and three on the head and neck (11%). The mean Breslow thickness was 3.2 mm (range 0.4–12). None of the patients had a family history of melanoma, one patient had a personal history of melanoma, and only three patients (11%) had multiple naevi (Table S1; see Supporting Information).

Clinically, NeMs most commonly presented as a nodule (16 of 27, 59%), followed by the plaque type (eight, 30%) and the papular type (three, 11%). Clinically, 10 cases of NeM

(37%) revealed two colours, with pink/red and brown being the most common. Eight (30%) were completely red, four (15%) were light brown, three (11%) were skin coloured and two (7%) were blue.

### Dermoscopic analysis

The global dermoscopic pattern of each NeM could be classified into one of three distinct types: (i) naevus-like tumours ( $n = 13$ , 48%): lesions typified by a papillomatous surface resembling a dermal naevus on clinical inspection and revealing a cobblestone pattern on dermoscopy; (ii) amelanotic tumours ( $n = 8$ , 30%): lesions lacking significant pigmentation clinically and dermoscopically; and (iii) tumours with a multicomponent pattern ( $n = 4$ , 15%): lesions revealing the classical melanoma-specific clinical and dermoscopic criteria.



Two lesions (7%) could not be classified into any pattern and were thus classified as mixed-pattern tumours.

Frequencies of the local dermoscopic features stratified according to these three groups are shown in Table 1. Naevus-like melanomas revealed predominantly irregular dots/globules (46%), atypical vascular pattern (46%), multiple milia-like cysts (38%), dotted vessels (31%), linear irregular vessels (31%) and irregular pigmentation (15%) (Fig. 3).

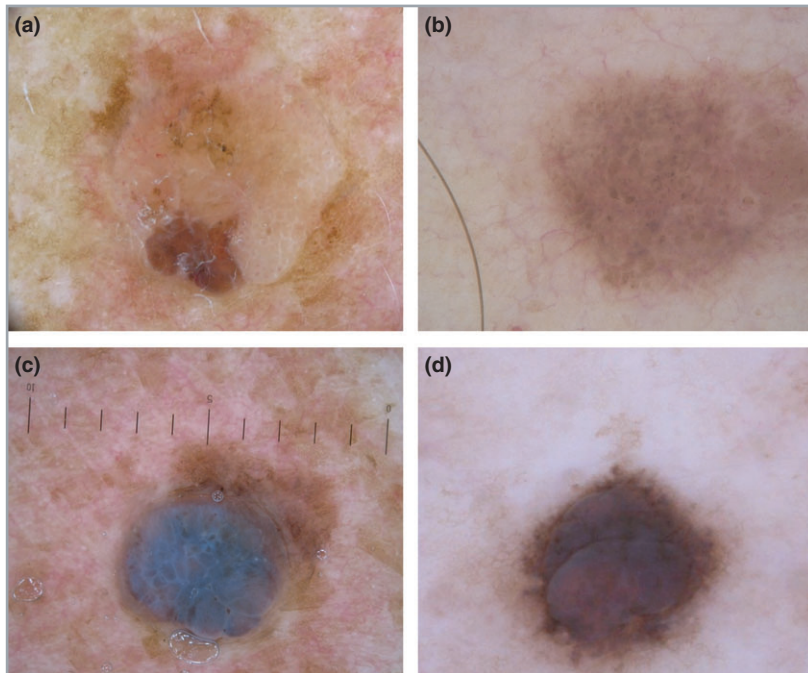
In the amelanotic category the NeMs revealed predominantly atypical vessels (75%), followed by dotted (38%) and glomerular vessels (38%). In three amelanotic lesions (38%), multiple milia-like cysts were also present. Interestingly, comma vessels, which are commonly seen in intradermal naevi, were not observed in NeMs (Fig. 4).

The third group, revealing a multicomponent pattern, showed the presence of dermoscopic features usually observed

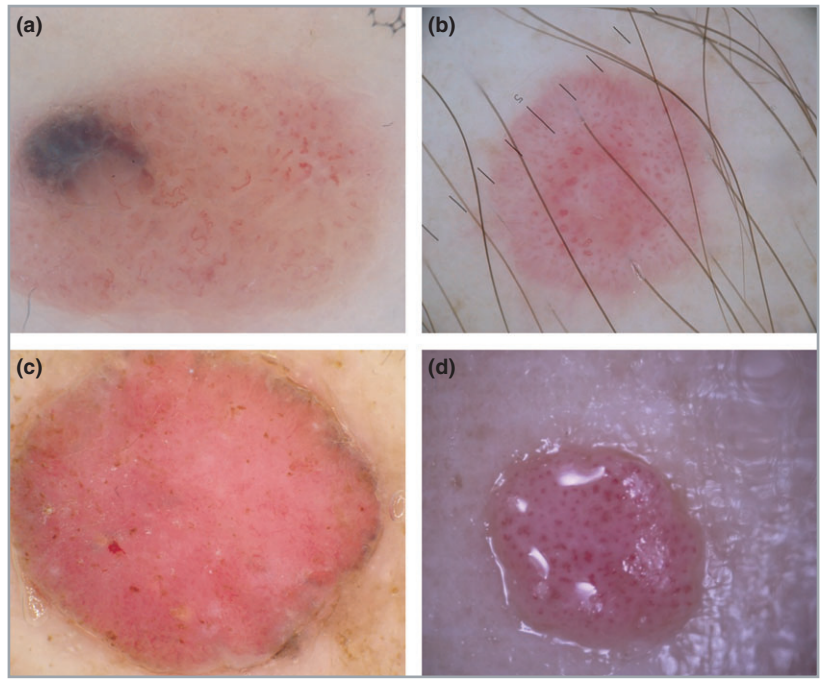
**Table 1** Absolute and relative frequencies of dermoscopic features according to distinct groups

Local dermoscopic feature	Naevus like, n = 13	Amelanotic, n = 8	Multicomponent, n = 4	Not categorized, n = 2
Comedo-like openings	0	0	0	0
Milia-like cysts	5 (38)	3 (38)	1 (25)	1
Arborizing vessels	0	0	0	0
Blue-grey ovoid structures	0	0	0	0
Red lacunae	0	1 (12)	0	0
Hairpin vessels	0	0	0	0
Glomerular vessels	0	3 (38)	1 (25)	0
Dotted vessels	4 (31)	3 (38)	0	0
Linear irregular vessel	4 (31)	4 (50)	0	0
Comma vessels	0	0	0	0
Atypical network	1 (8)	0	1 (25)	0
Irregular streaks	1 (8)	0	0	0
Irregular dots	6 (46)	0	1 (25)	1
Blue veil	0	0	3 (75)	2
Regression	0	0	0	0
Irregular pigmentation	2 (15)	0	3 (75)	0
Atypical vascular pattern	6 (46)	6 (75)	1 (25)	0

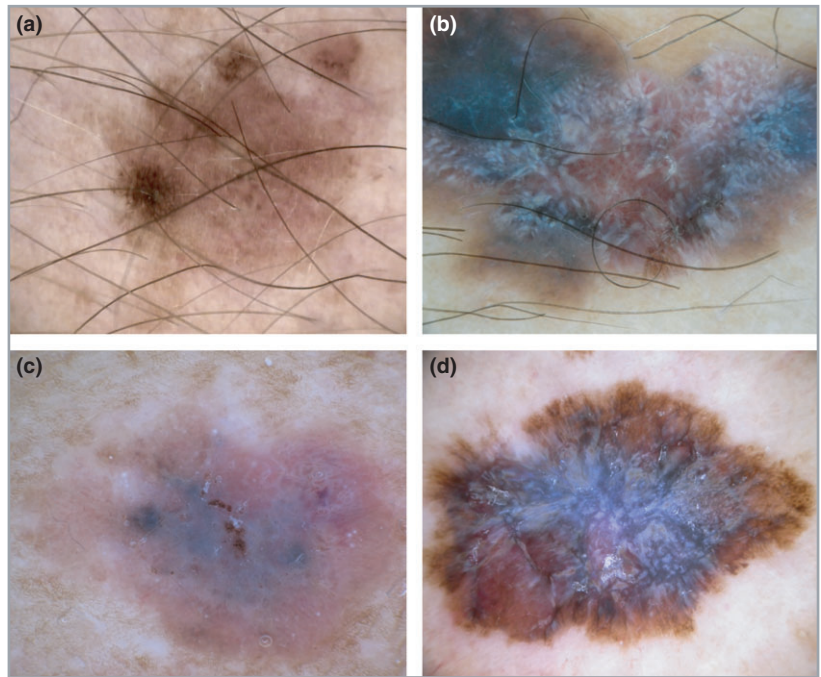
Values are n (%).



**Fig 3.** Naevus-like naevoid melanoma. All lesions show a naevus-like appearance with colours varying from skin-coloured (a) to light brown (b), bluish (c) and reddish brown (d). Irregular pigmentation (a, c) and irregularly distributed globules (b, d) are observed. Original magnification  $\times 20$ .



**Fig 4.** Amelanotic naevoid melanoma. An atypical vascular pattern is observed in all tumours, consisting of linear irregular vessels or serpentine (a), dotted (b, c) or glomerular vessels (d). Multiple milia-like cysts are seen in lesion (c). Original magnification  $\times 20$ .



**Fig 5.** Naevoid melanoma tumours revealing a multicomponent pattern. Melanoma-specific criteria are seen in these tumours, such as the presence of an atypical network (a, d) and blue veil (b–d). Original magnification  $\times 20$ .

in superficial spreading melanoma, such as blue-white veil (75%), irregular pigmentation (75%) and atypical network (25%) (Fig. 5).

Of the two lesions that could not be classified into one of the patterns mentioned above, one revealed spitzoid dermoscopic features, with a symmetric shape and globules irregularly distributed throughout the lesion, and the second showed structureless pigmentation and sharp borders resembling a seborrhoeic keratosis.

## Discussion

NeM refers to a rare variant of melanoma that can clinically resemble a naevus. Avoiding the misdiagnosis of NeM requires expertise in recognizing the subtle clinical and histopathological features common to NeM.

Clinically, NeM has been described as a brown nodule located on the trunk or proximal limbs of young adults.<sup>1–19</sup> Consistent with the literature,<sup>2–14</sup> in our study there was a

male predominance (59%) and a mean age of 51.5 years, with most of the lesions located on the trunk and extremities. Overall, our patients with NeM had a low-risk phenotype with few naevi, and a negative personal and family history of melanoma (Table S1; see Supporting Information).

Dermoscopically, most NeMs could be classified as having one of three global patterns: naevus-like, amelanotic type and multicomponent type. The naevus-like type includes lesions with clinical and dermoscopic morphology resembling a naevus with a papillomatous or mammilated surface. The stereotypical dermoscopic feature of an intradermal naevus is the presence of a globular, cobblestone or structureless pattern, often associated with thick comma-like (linear curved) vessels.<sup>28–30</sup> These naevi are usually homogeneously pigmented, with colour varying from skin coloured to light and dark brown.<sup>30</sup> In our study, NeMs simulating intradermal naevi on histopathology had two clinical morphological extremes, with some lesions manifesting a papillomatous surface and others displaying the classical features of melanoma. However, most of the NeMs did have an atypical vascular pattern with polymorphic vessels. This observation is in accordance with previous reports demonstrating that the presence of comma-like vessels is a negative predictor for the diagnosis of melanoma.<sup>24</sup> Another feature often associated with benign lesions, which was found in our cases, was milia-like cysts. Despite the presence of features often associated with benign lesions (papillomatous topography, comma vessels and milia cysts), most of the naevus-like NeMs had an irregularly distributed pigmentation and irregular dots/globules. These features often helped to increase the index of suspicion that the lesion under investigation was a melanoma.

The second group of NeMs included amelanotic, symmetric papules or nodules characterized by the presence of an atypical vascular pattern consisting of linear irregular (serpentine), dotted and/or glomerular vessels. Thus, although the overall clinical morphology is that of a clinically banal-appearing lesion, the presence of atypical vascularity seen with dermoscopy can help in identifying these NeMs. In a previous study on amelanotic melanomas the presence of atypical vascular patterns<sup>24</sup> was found to be the most predictive feature for amelanotic melanoma, and included the following: predominant centrally located vessels, hairpin vessels, milky red to pink areas, more than one shade of pink, a combination of dotted and linear irregular vessels, and linear irregular vessels as the predominant vessel type. In the amelanotic subtype of NeM, the predominant pattern was linear irregular (50%), followed by dotted (38%) and glomerular vessels (38%).

The third group of NeMs, typified by a multicomponent pattern, did not show any distinctive morphological differences from what has already been described for superficial spreading melanoma.<sup>31</sup> Dermoscopically, they were characterized by the presence of multiple colours, blue-white veil, irregular dots/globules and irregular pigmentation. All of these features are strongly associated with the diagnosis of melanoma, and thus these NeMs are usually not diagnostically challenging for the clinician.

Our study has some limitations. Firstly, it involves a relatively small number of cases, although NeM represents a rare tumour variant and thus it is quite difficult to obtain a larger study population. Secondly, it was not possible to classify two tumours (7% of cases) into any of the above-mentioned categories, as one lesion was typified by a spitzoid appearance and the other simulated a seborrhoeic keratosis. Thirdly, the diagnostic accuracy of dermoscopy to differentiate NeMs from other melanoma subtypes or from common naevi was not tested, and prospective larger studies are needed.

In conclusion, while NeMs may be difficult to differentiate from naevi based on naked-eye visual examination, dermoscopy may provide clues to help identify this malignancy. Our study highlights that the most common dermoscopic features found in NeMs include atypical vessels and irregular dots/globules.

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