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Nodular melanoma: five consecutive cases in a general practice with polarized and non-polarized dermatoscopy and dermatopathology

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ABSTRACT

Background: The incidence of nodular melanoma (NM) has been consistently described as at least 10-15% of total melanomas for over 15 years despite advances in diagnostic algorithms and medical technology. NMs are strongly correlated with faster rates of growth and poorer prognosis and thus provide clinicians with a challenge for early recognition.

Objective: To evaluate diagnostic clues of consecutive histopathologically proven NMs in one general practice with particular emphasis on dermatoscopic characteristics and compare this to the published literature.

Method: A retrospective observational study was performed of five consecutive histologically proven NM, from a total of 212 consecutive melanomas from a general practice in Brisbane, Queensland, Australia. Dermatoscopic images, both polarized and non-polarized, which appears to be a unique resource, and dermatopathologic slides were available for all lesions.

Results: All of the NMs in this series were pigmented although one was hypomelanotic. Two of them were symmetrical. The most highly sensitive clues to NM were gray or blue structures and polarizing-specific white lines.

Limitations: Due to the small number of NMs in this report no statistical significance can be attributed to the observational findings.

Conclusion: This small series supports what is already known: that a significant proportion of NMs may be dermatoscopically symmetrical but that known clues to melanoma are frequently present. Nodular lesions, pigmented or non-pigmented, should be excised to exclude NM if there is any clue to malignancy, regardless of symmetry, unless a confident specific benign diagnosis can be made.

Introduction

Nodular melanoma (NM), defined as a melanoma with any junctional component extending no more than three rete ridges beyond the invasive component, is the second largest melanoma subtype, comprising 10-15% of melanomas in Caucasians [1]. NMs have been shown to have a faster growth rate (GR) (median GR 0.49 mm/month) than lentigo maligna melanomas (median GR 0.13 mm/month) and superficial spreading melanomas (SSM) (median GR 0.12 mm/month) [2]. The GR of malignant melanomas (MM) has also been shown to be an independent prognostic indicator for the prediction of relapse after one year of follow up [3]. Studies have been performed in an attempt to determine diagnostic features, both clinical and dermatoscopic, which facilitate earlier diagnosis of NM, when Breslow thickness is less and prognosis therefore more favorable [4]. A general practice, with a special interest in skin cancer medicine and dermatoscopic photo-documentation of all treated lesions, provides a unique perspective on the evaluation of this condition.

Methods

A retrospective analysis was performed with respect to all NMs diagnosed between January 1, 2008, and June 30, 2013, in a general practice in Brisbane, Queensland, Australia. All lesions treated were prospectively recorded on the Skin Cancer Audit Research Database (SCARD) for both tracking and research purposes [5]. During the time interval of this study, five NMs were diagnosed from a total of 212 melanomas, 163 (76.8%) in-situ and 49 (23.2%) invasive. The percentage of melanomas which were nodular was therefore 2.4% of total melanomas and 10.2% of invasive melanomas. From January 1, 2008, to June 30, 2013, the 'Number Needed to Treat' (NNT) with respect to all melanomas diagnosed in this practice, calculated from the prospectively declared intention to confirm or exclude melanoma, was 5.36 [6].

Photo-documentation was routinely performed on all lesions submitted for histopathology, including clinical, macro and dermatoscopic images. Dermatopathologic copy-slides were also collected, catalogued and where appropriate, photographed. Dermatoscopic images were taken of all cases with a DermLite Fluid non-polarizing dermatoscope (3Gen, LLC) coupled to a Canon 50D digital camera (Canon USA, Inc.) and after October 2010, also with either a DermLite II HR polarized or DermLite DL3 (polarized and non-polarized) dermatoscope (3Gen, LLC) coupled to an Olympus E-450 digital camera (Olympus Corporation). Both non-polarized and polarized dermatoscopic images were available for each of the five NM.

Cases

The five cases of histologically diagnosed NM are presented in Tables 1 and 2 with relevant clinical, dermatoscopic and dermatopathologic information. In estimation of melanoma growth rate (GR) we used the ratio MM thickness/duration of the MM visible growth as defined in a previously described assessment tool [3]. Clinical images are displayed in Figure 1, close-up images in Figure 2 and dermatoscopic and dermatopathologic images of each lesion are displayed in Figures 3 to 7.

TABLE 1. Patient discovery and lesion details of a series of five consecutive nodular melanomas in a general practice.*

Case	Sex	Age	Skin Type	Previous Melanoma	Self Discovered	Diameter (mm)	Breslow (mm)	Mitotic rate (mm/square)	Ulceration	Growth rate (mm/month)
1	M	42	3	no	yes	4	1.35	5	yes	1.30
2	M	75	3	no	yes	11	5.00	9	yes	3.30
3	M	85	1	no	yes	10	3.80	4	yes	5.10
4	M	58	1	yes	yes	4	0.82	1	yes	1.09
5	F	62	2	no	no	3	0.90	1	no	N/K

*Growth rate (GR) is calculated according to a previously published calculation tool as melanoma thickness divided by the duration of visible melanoma growth. The GR was Case 5 was not known as the patient had no knowledge of the lesion. [Copyright: ©2014 Rosendahl et al.]

TABLE 2. Dermatoscopy features of the series of five consecutive nodular melanomas listed in Table 1.*

Case	Asymmetry	Blue/Black Structures	Gray/Blue Structures	Lines white (non-polarized)	Lines white polarizing specific	Polymorphous vessels
1	yes	no	no	yes	yes	yes
2	no	yes	yes	yes	yes	yes
3	yes	no	yes	no	yes	yes
4	yes	yes	yes	no	yes	no
5	no	yes	yes	no	no	no

*Asymmetry is defined as asymmetry of structure or color and is based on pattern, not outline. Blue/black structures are defined as blue/black color covering at least 10% of the lesion. Gray or blue structures are rated if these colors are seen on any part of the lesion. White lines (non-polarized) are rated if seen with non-polarizing dermatoscopy. Polarizing-specific white lines are white lines, perpendicularly orientated to each other, seen only with polarized dermatoscopy and polymorphous vessels are defined as a pattern including more than one vessel type. [Copyright: ©2014 Rosendahl et al.]

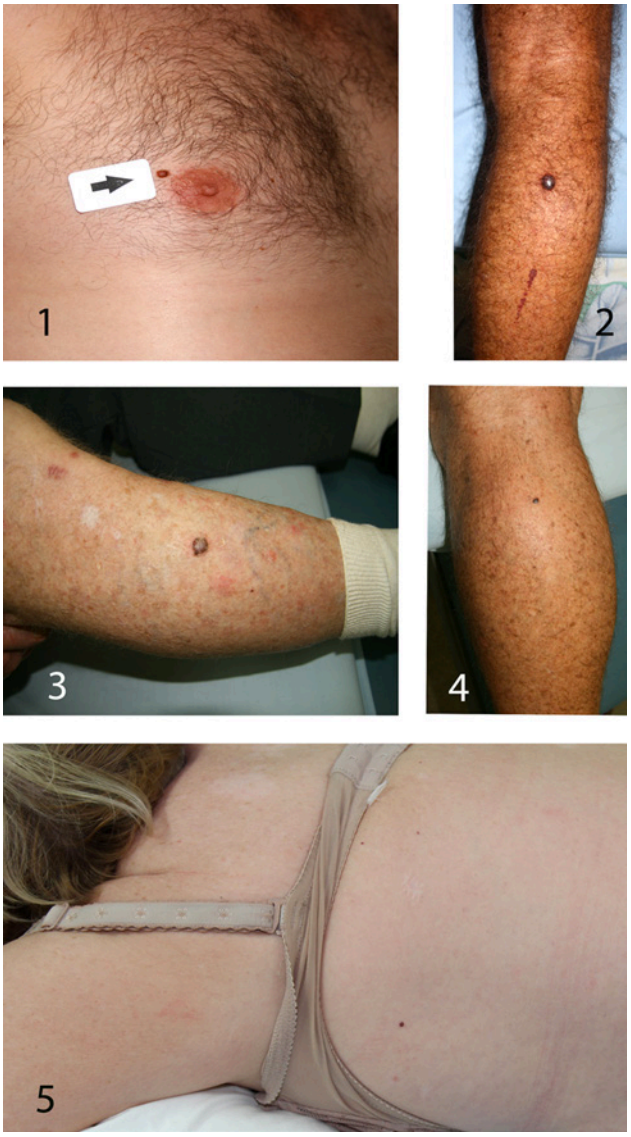

Figure 1. Clinical images of five consecutive nodular melanomas from a general practice. Case 1: A small brown nodule on non-sun-damaged skin adjacent to the right areola on a 42-year-old man. Case 2: A blue nodule on sun-damaged skin on the right upper calf of a 75-year-old man. Case 3: A brown nodule on sun-damaged skin on the right lateral leg of an 85-year-old man. Case 4: A small blue nodule on sun-damaged skin on the upper calf of a 58-year-old man. Case 5: A very small brown nodule on non-sun-damaged skin on the back of a 62-year-old woman. [Copyright: ©2014 Rosendahl et al.]

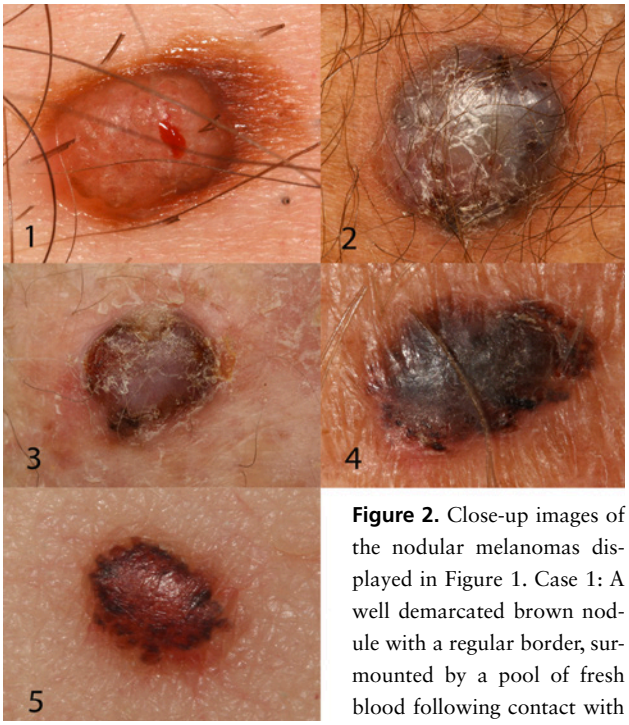

Figure 2. Close-up images of the nodular melanomas displayed in Figure 1. Case 1: A well demarcated brown nodule with a regular border, surmounted by a pool of fresh blood following contact with a dermatoscope footplate. There is macular brown pigment on three sides. Case 2: A well demarcated shiny blue nodule with a regular border, with surface scale. Case 3: A well demarcated brown nodule with surface scale, more lightly colored centrally, with an eccentric darker area at one part of the slightly irregular border. Case 4: A well demarcated black nodule with an irregular border. Case 5: A well demarcated irregularly pigmented brown and black nodule with a markedly irregular border. [Copyright: ©2014 Rosendahl et al.]

Discussion

The incidence of NMs in this study was 10.2% (n=5/49) of invasive melanomas comparing to 10-15% in published large studies [4].

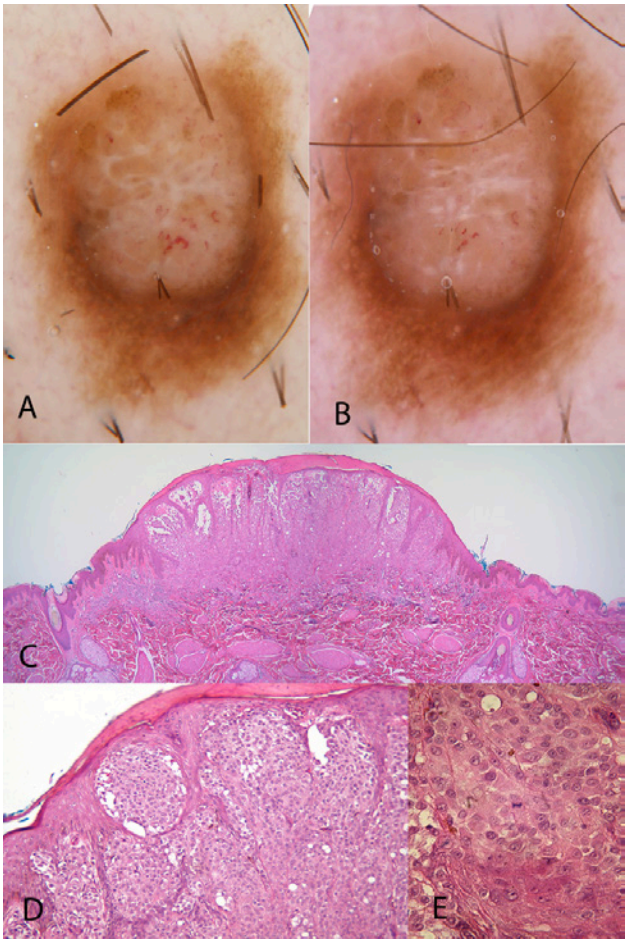

Figure 3. Case 1: (A) Non- polarized dermatoscopic image; (B) Polarized dermatoscopic image; (C, D and E) Dermatopathology images. White lines seen in both dermatoscopy images (perpendicularly orientated in the polarized image) arguably correlate with vertical bands of collagen seen in the dermatopathologic overview (C). A mitotic Figure is seen centrally in (E). [Copyright: ©2014 Rosendahl et al.]

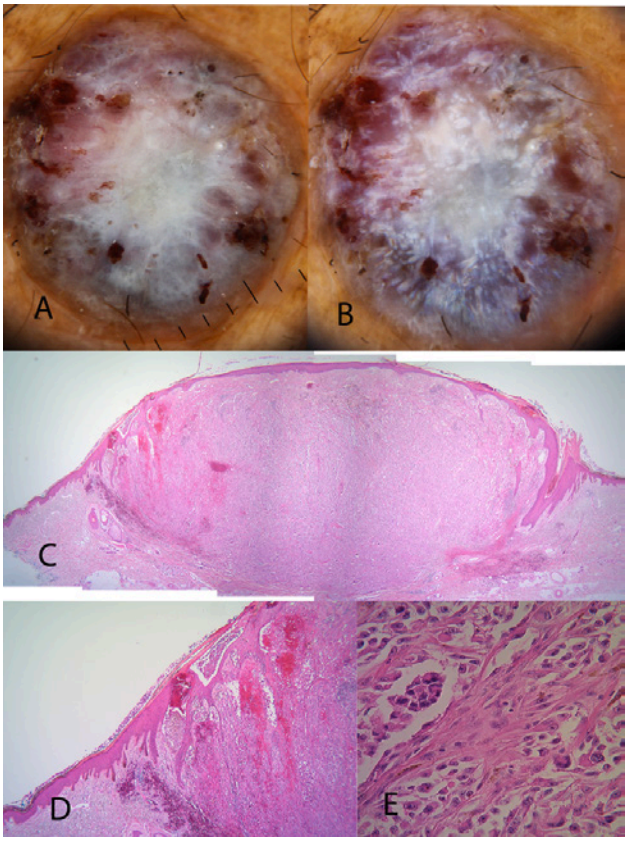

Figure 4. Case 2: (A) Non- polarized dermatoscopic image; (B) Polarized dermatoscopic image; (C, D and E) Dermatopathology images. The polarizing-specific perpendicular white lines are concentrated peripherally (B) and arguably correlate with vertical bands of collagen seen peripherally in the dermatopathologic images (C and D). [Copyright: ©2014 Rosendahl et al.]

One study of 1789 patients with melanoma found that NM was most frequently found in older men and most commonly on the lower limbs or head and neck [7]. In addition, it was shown to be more strongly correlated with actinic keratosis rather than high nevi counts [7]. This suggests that NMs have an association with sun-damaged skin. In our series 80% (n= 4/5) were male and 75% (n=3/4) of these males were over 50. With respect to body site, 60% (n=3/5) were on the leg (on sun-damaged skin) and 40% (n=2/5) were on the torso (on non-sun-damaged skin).

In a study involving 92 SSMs and 33 NMs, a higher proportion of NM was discovered by the patient (60.6%) compared to SSM (48.9%) [8], and in a study of 22 patients with NM, 61% were first detected by the patient and another 17% detected by another family member and the patient [9]. In our series 60% (n= 3/5) were reported by the patient and another was known of by the patient, but this information was not volunteered until after the lesion was discovered (Case 4). In one case where the lesion was only 3 mm in diameter and on the posterior torso, it was discovered by the doctor without the patient having any prior awareness of it (Case 5). This compares to the non-nodular melanomas in the same practice where only 9.6% (n= 20/207) were discovered by the patient (of the remainder 14 were discovered by another doctor, 5 by another person and the remainder by the treating practitioner). We believe that this highlights the importance of patient education and awareness in the recognition of abnormal changes in skin lesions but it also illustrates the value of a clinician proceeding to examine the total skin surface when presented with any lesion of concern.

The clinical ABCD method is the most widely known algorithmic method for the clinical diagnosis of melanoma and has been promoted both to healthcare professionals and patients [10]. One of the criteria for melanomas to be detected using this method is that they have a minimum diameter of 6 mm. It has been agreed among many authors that a significant proportion of NMs do not fulfil the ABCD criteria including the criterion of a minimum lesion size of 6mm [8,11]. In one series of eleven thin NMs (Breslow thickness 2 mm or less), 63.6% (n=7/11) had a diameter of less than 6 mm [4]. Similarly, in our series 60% (n=3/5) had a diameter less than 6mm and furthermore, each of these also had a Breslow thickness less than 2 mm.

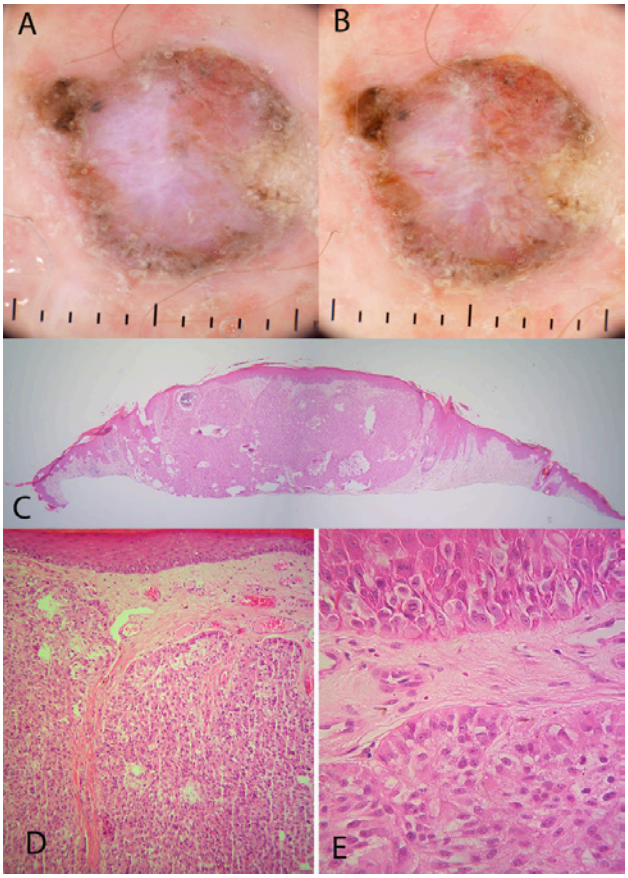

Figure 5. Case 3: (A) Non- polarized dermatoscopic image; (B) Polarized dermatoscopic image; (C, D and E) Dermatopathology images. Polarizing-specific white lines are seen centrally (B) and arguably correlate with dermatopathologic vertical collagen bands, not apparent in the overview (C) but seen in the central part of the lesion in the higher power view (D). [Copyright: ©2014 Rosendahl et al.]

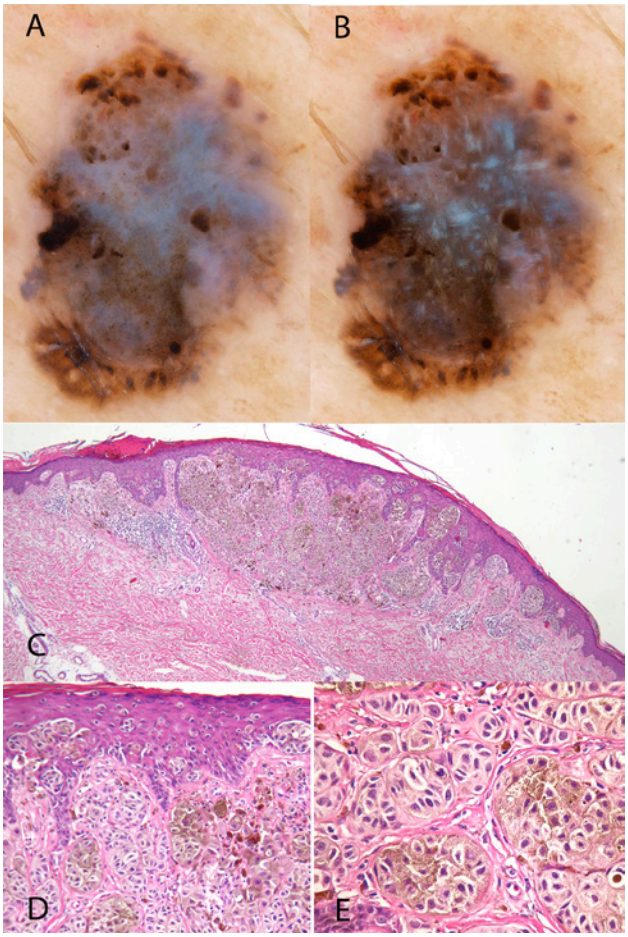

Figure 6. Case 4: (A) Non- polarized dermatoscopic image; (B) Polarized dermatoscopic image; (C, D and E) Dermatopathology images. Heavily pigmented melanocytes concentrated in the dermis correlate with the structureless blue, caused by the Tyndall effect, seen in (A) and pagetoid nests and single cells in the epidermis correlate with black clods and dots respectively seen in both (A) and (B). Polarizing-specific blue-white lines seen in (B) arguably correlate with vertical bands of collagen seen in (D). [Copyright: ©2014 Rosendahl et al.]

With respect to dermatoscopic examination there were some similarities between the melanomas in our series (see Table 2) and those in larger published studies.

It has been shown that in NM many of the classic dermatoscopic features of SSM are lacking, however, irregularity of color is usually present in those that do contain pigment [12]. All of the melanomas in our series contained melanin pigment, although in one (Case 3) 75% of the lesion was non-pigmented and this would categorize it as an amelanotic/hypomelanotic melanoma (AHM) [13].

In our series symmetry was present in 40% (n=2/5; Cases 2 and 5) and if the accompanying nevus was ignored Case 1 was also symmetrical; all were pigmented. The asymmetrical melanomas in our series were asymmetrical in both structure and color. In a published series of 33 NMs, 80% were symmetrical and 60.7% were classified as amelanotic [8]. In another published study 64% (n=7/11) of thin NMs (Breslow 2 mm of less) were symmetrical and 18% (n=2/11) were classified as amelanotic [4].

A study of a series of 283 nodular pigmented lesions found that the presence of blue/black color covering at least 10% of the lesion had 78.2% sensitivity for melanoma [14]. The clue of 'blue-black color' was present in 60% (n=3/5) of the NMs in our series.

The clues to malignancy of gray or blue structures and polarizing specific white lines (defined as perpendicularly orientated white lines visible only on polarized dermatoscopy) displayed the highest sensitivity for NM in our small consecutive series; each of them (n=5/5) had either one or the other clue and 60% (n=3/5) had both.

Polarizing-specific white lines were first named 'chrysalis structures' [15] and were attributed to the presence of increased collagen, which has birefringent properties causing rapid randomization of polarized light thus making the collagen more conspicuous. In a study by Balagula et al. it was found that in non-biopsied lesions these structures were most commonly found in dermatofibromas and scars, but in 265 biopsied lesions including 20 melanomas they were observed

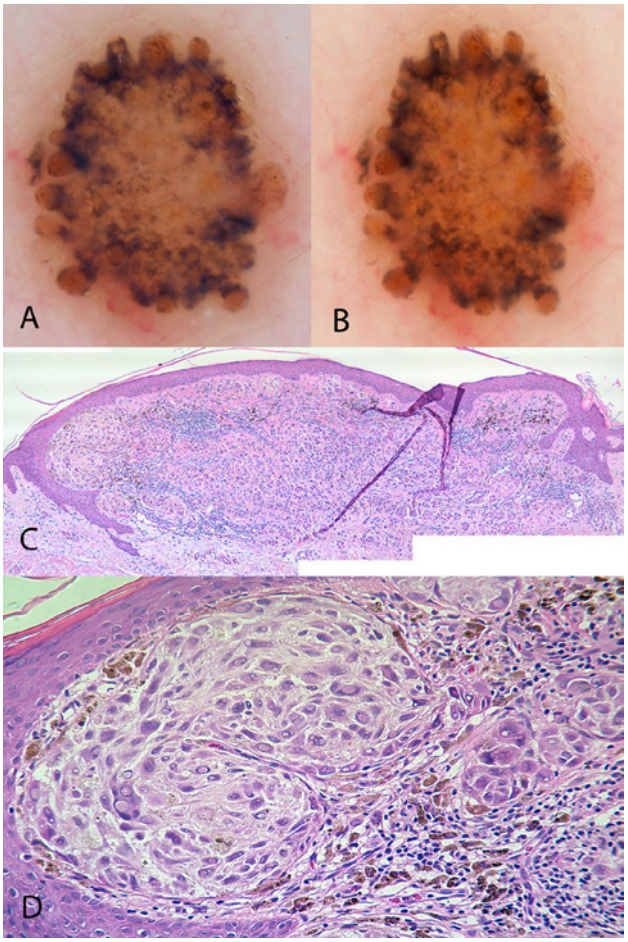

Figure 7. Case 5: (A) Non- polarized dermatoscopic image; (B) Polarized dermatoscopic image; (C and D) Dermatopathology images. There are no dermatoscopic polarizing-specific white lines (B), and consistent with the hypothesis that these structures correlate to vertical collagen bands, none of these are seen in the dermatopathologic images although abundant collagen surrounds nests of melanocytes (C and D). On the extreme left side (C and shown at high power in D) an eccrine duct can be seen attenuated by a large melanocyte nest which appears to be bulging into it. This would correlate with a dermatoscopic peripheral brown clod, as there is no apparent collagen within or superficial to this nest to induce the Tyndall effect. [Copyright: ©2014 Rosendahl et al.]

in 47.6% of basal cell carcinomas and 84.6% of invasive melanomas [16]. They were found to be more frequently observed in invasive melanomas than in-situ melanomas and their prevalence correlated to increased thickness of melanomas. In our series of 212 melanomas (23.2% n=49 invasive), both polarized and non-polarized dermatoscopy images were available in 142 (19.7% n=28 invasive). While 80% (n=4/5) of the nodular melanomas had polarizing-specific white lines only 7.2% (n=10/137) of the non-nodular melanomas displayed this feature and all but one of those were in-situ.

In Case 1 of our series the polarizing-specific white lines appear to correlate with white lines also seen with non-polarized dermatoscopy and we speculate that they correlate with vertical bands of collagen seen in the dermatopathology image (Figure 3C). In Case 2, polarizing specific white lines are seen peripherally (centrally is structureless white) and vertical collagen bands are seen peripherally in the dermatopathology image (Figure 4D). In Case 3 no white lines are seen in the non-polarizing image—just a white structureless area—but they are seen centrally in the polarized image. Correspondingly, vertical collagen bands, while not conspicuous in the low power view, are seen centrally in the medium-high power view (Figure 5D). In Case 4 the polarizing-specific lines are actually blue/white and there are no white or blue lines in the non-polarized view, just a very prominent structureless blue area. There is an abundance of collagen evident in the dermatopathology images of this case and significant vertical orientation of this is seen in the medium-high power view (Figure 6D). Case 5 is the exception in our series and contains no dermatoscopic white lines in either the polarized on non-polarized images. Of significance, no vertically oriented bands of collagen are seen in any of the dermatopathological images of this case.

We believe this supports the hypothesis that polarizing-specific white lines represent increased collagen production as vertically orientated bands, probably reflecting increased fibroblast activity related to the vertical growth phase of melanoma [16].

Conclusion

NM is a subtype of melanoma distinct from SSM both dermatopathologically and in its biological behavior. The presentation of five consecutive NMs with both polarized and non-polarized dermatoscopy provides a unique perspective on this lesion and supports what is already known: that a significant proportion of nodular melanomas may be dermatoscopically symmetrical but that known clues to melanoma are frequently present. Every one of these five NMs, whether symmetrical or not, had either gray/blue color or polarizing-specific white lines or both. The hypothesis that perpendicular white lines correlate to vertical bands of collagen related to the growth dynamics of invasive melanoma is supported by the fact that the four NMs in our series which displayed dermatoscopic polarizing-specific white lines also displayed dermatopathologic vertical bands of collagen in the dermis, while the one that did not have this feature had no dermatopathologic vertical collagen bands.

We would suggest that more NMs would be diagnosed earlier if nodular lesions with any known clue to malignancy were considered for biopsy regardless of symmetry. In particular, the clue of polarizing-specific white lines should lead to excision unless a confident specific benign diagnosis, for example, of dermatofibroma, can be made on historic and clinical grounds.

References

1. Porras BH, Cockerell CJ. Cutaneous malignant melanoma: classification and clinical diagnosis. Semin Cutan Med Surg. 1997 Jun;16(2):88–96.
2. Liu W, Dowling JP, Murray WK, et al. Rate of growth in melanomas: characteristics and associations of rapidly growing melanomas. Arch Dermatol. 2006 Dec;142(12):1551–8.
3. Grob JJ, Richard MA, Gouvernet J, et al. The kinetics of the visible growth of a primary melanoma reflects the tumor aggressiveness and is an independent prognostic marker: a prospective study. Int J Cancer. 2002 Nov 1;102(1):34–8.
4. Kalkhoran S, Milne O, Zalaudek I, et al. Historical, clinical, and dermoscopic characteristics of thin nodular melanoma. Arch Dermatol. 2010 Mar;146(3):311–8.
5. Rosendahl C, Hansen C, Cameron A, et al. Measuring performance in skin cancer practice: the SCARD initiative. Int J Dermatol. 2011 Jan;50(1):44–51.
6. Rosendahl C, Williams G, Eley D, et al. The impact of subspecialization and dermatoscopy use on accuracy of melanoma diagnosis among primary care doctors in Australia. J Am Acad Dermatol. 2012 Nov;67(5):846–52.
7. Chamberlain AJ, Fritschi L, Giles GG, Dowling JP, Kelly JW. Nodular type and older age as the most significant associations of thick melanoma in Victoria, Australia. Arch Dermatol. 2002 May;138(5):609–14.
8. Chamberlain AJ, Fritschi L, Kelly JW. Nodular melanoma: patients' perceptions of presenting features and implications for earlier detection. J Am Acad Dermatol. 2003 May;48(5):694–701.
9. Bergenmar M, Hansson J, Brandberg Y. Detection of nodular and superficial spreading melanoma with tumour thickness < or = 2.0 mm—an interview study. Eur J Cancer Prev. 2002 Feb;11(1):49–55.
10. Friedman RJ, Rigel DS, Kopf AW. Early detection of malignant melanoma: the role of physician examination and self-examination of the skin. CA Cancer J Clin 1985;35(3):130-51.
11. Kelly JW, Chamberlain AJ, Staples MP, McAvoy B. Nodular melanoma. No longer as simple as ABC. Aust Fam Physician. 2003 Sep;32(9):706–9.
12. Segura S, Pellacani G, Puig S, et al. In vivo microscopic features of nodular melanomas: dermoscopy, confocal microscopy, and histopathologic correlates. Arch Dermatol. 2008 Oct;144(10):1311–20.
13. Moloney FJ, Menzies SW. Key points in the dermoscopic diagnosis of hypomelanotic melanoma and nodular melanoma. J Dermatol. 2011 Jan;38(1):10–5.
14. Argenziano G, Longo C, Cameron A, et al. Blue-black rule: a simple dermoscopic clue to recognize pigmented nodular melanoma. Br J Dermatol. 2011;165(6):1251-5.
15. Marghoob AA, Cowel L, Kopf AW, Scope A. Observation of chrysalis structures with polarized dermoscopy. Arch Dermatol. 2009 May 1;145(5):618.
16. Balagula Y, Braun RP, Rabinovitz HS, et al. The significance of crystalline/chrysalis structures in the diagnosis of melanocytic and nonmelanocytic lesions. J Am Acad Dermatol. 2012 Aug;67(2):194.e1–8.