ONLINE FIRST

Dermoscopic Evaluation of Nodular Melanoma

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Importance: Nodular melanoma (NM) is a rapidly progressing potentially lethal skin tumor for which early diagnosis is critical.

Objective: To determine the dermoscopy features of NM.

Design: Eighty-three cases of NM, 134 of invasive non-NM, 115 of nodular benign melanocytic tumors, and 135 of nodular nonmelanocytic tumors were scored for dermoscopy features using modified and previously described methods. Lesions were separated into amelanotic/hypomelanotic or pigmented to assess outcomes.

Setting: Predominantly hospital-based clinics from 5 continents.

Main Outcome Measures: Sensitivity, specificity, and odds ratios for features/models for the diagnosis of melanoma.

Results: Nodular melanoma occurred more frequently as amelanotic/hypomelanotic (37.3%) than did invasive non-NM (7.5%). Pigmented NM had a more frequent (compared with invasive non-NM; in descending order of odds ratio) symmetrical pigmentation pattern (5.8% vs 0.8%), large-diameter vessels, areas of homogeneous blue pigmentation, symmetrical shape, predominant peripheral vessels, blue-white veil, pink color, black color, and milky red/pink areas. Pigmented NM less frequently displayed an atypical broadened network, pigment network or pseudonetwork, multiple blue-gray dots, scarlike depigmentation, irregularly distributed and sized brown dots and globules, tan color, irregularly shaped depigmentation, and irregularly distributed and sized dots and globules of any color. The most important positive correlating features of pigmented NM vs nodular nonmelanoma were peripheral black dots/globules, multiple brown dots, irregular black dots/globules, blue-white veil, homogeneous blue pigmentation, 5 to 6 colors, and black color. A model to classify a lesion as melanocytic gave a high sensitivity (>98.0%) for both nodular pigmented and nonnodular pigmented melanoma but a lower sensitivity for amelanotic/hypomelanotic NM (84%). A method for diagnosing amelanotic/hypomelanotic malignant lesions (including basal cell carcinoma) gave a 93% sensitivity and 70% specificity for NM.

Conclusions and Relevance: When a progressively growing, symmetrically patterned melanocytic nodule is identified, NM needs to be excluded.

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NODULAR MELANOMA (NM) is defined as an invasive melanoma that lacks significant intraepidermal tumor cells beyond the margins of the dermal invasive component.[1] Although NM constitutes only 9% to 15% of invasive melanoma, it is overrepresented as a cause of lethal melanoma. Nodular melanoma is the most frequent subtype of thick, rapidly growing melanomas (reviewed by Chamberlain and Ng[2] and Kelly et al[3]), is frequently not diagnosed until it is at a locally advanced stage, and therefore is associated with a relatively poor prognosis. The lesions present clinically as firm papules or nodules, with more frequent ulceration and less color variegation than other invasive melanomas. Nodular melanoma lesions are more frequently light colored than the other common melanoma subtypes. For

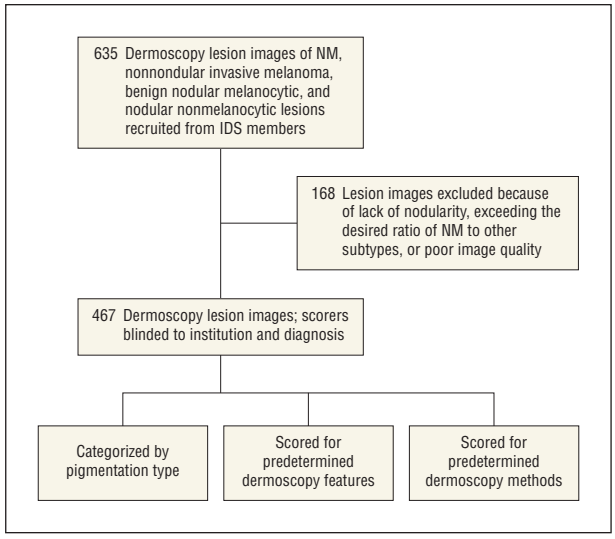

Figure 1. Flowchart of included lesions. IDS indicates International Dermoscopy Society; NM, nodular melanoma.

this reason, the well-known ABCD rule (*a*symmetry, *b*order irregularity, *c*olor variability, and *d*iameter >6 mm) for clinical diagnosis for NM is less useful, and an EFG pneumonic of *e*levation, *f*irm consistency, and progressive *g*rowth to describe their clinical presentation is more apt.[3] In Australia, NM lesions are more commonly found in sun-damaged skin of the head and neck region of elderly men.[2]

Unlike the extensive literature on the dermoscopy of melanoma in general, there is a relative paucity of dermoscopy literature on the subtype NM,[4-6] with many observations grouped with those of other invasive melanomas[7] or small case series.[8,9] In this study, we documented the dermoscopy features of a large series of NM; we describe that here and validate criteria used for their dermoscopic diagnosis.

METHODS

IMAGE ACQUISITION AND INCLUSION AND EXCLUSION CRITERIA

Digital dermoscopic images of lesions taken with glass plate/liquid nonpolarized or cross-polarized photographic devices were obtained from members of the International Dermoscopy Society from 5 continents. A request was made for images of all NMs satisfying the inclusion criteria and for a random selection of nonnodular invasive primary melanoma, benign nodular melanocytic lesions, and nodular nonmelanocytic lesions at a desired ratio of NM to other subgroups of 1:2.

All lesions obtained were excised and histopathologic examination was performed except for some benign melanocytic nevi that showed no change over time compared with baseline photographs. Nodular melanoma was defined as an invasive melanoma without an in situ (junctional) component beyond 3 rete ridges of the dermal invasive component.[1] The histologic sections of all NM lesions were reviewed by a second pathologist either at the institution of origin or by one of us (R.A.S.). Lesions were included as "nodular" melanoma only when the second review confirmed the diagnosis according to the histologic definition used. Both nodular benign melanocytic lesions and nodular nonmelanocytic lesions were identified by the clinical appearance of a solitary nodule and confirmed using dermoscopic examination.

Table 1. Frequency of Diagnosis

Diagnosis	Frequency, No.
Invasive melanoma	217
Nodular melanoma	83
Superficial spreading melanoma	133
Lentigo maligna melanoma	1
Benign melanocytic lesions	115
Common nevi	87
Spitz nevi	12
Blue nevi	15
Deep penetrating nevi	1
Nonmelanocytic lesions	135
Basal cell carcinoma	62
Seborrheic keratosis	34
Hemangioma	11
Dermatofibroma	11
Other	17

Images received were included, attempting to maintain the desired ratio of 1:2 for nodular malignant melanoma (MM) to other subtypes within individual centers (M.A.), and confirmed as morphologically nodular and correctly categorized according to their histopathologic examination reports (P.G. and M.A.). These dermoscopic images were reviewed (S.W.M.), blinded to diagnosis and institution of origin, categorized by their pigmentation type as previously reported,[7] and excluded if the image quality was poor. Amelanotic lesions were defined as having no melanin pigmentation (ie, tan, dark brown, blue, gray, or black) on dermoscopic examination. Tan pigmentation is defined as light brown pigmentation that is darker than the surrounding skin. Two subgroups of hypomelanotic lesions were defined. On dermoscopic evaluation, partially pigmented lesions have a melanin pigmentation area of less than 25% of the total surface area. Light-colored (slightly pigmented) lesions have only tan, light blue, or light gray pigmentation that may occupy more than 25% of the total surface area; no dark brown, deep blue, or black pigmentation is found. All lesions not categorized as amelanotic or hypomelanotic by these definitions were defined as "pigmented." The flowchart of included lesions is shown in **Figure 1**.

The study consisted of 467 lesions; of these, 83 were NM, 134 were invasive non-NM, 115 were nodular benign melanocytic tumors, and 135 were nodular nonmelanocytic tumors. **Table 1** reports the frequency of each diagnosis, and **Table 2** lists the frequency of each major diagnostic category as a function of the overall dermoscopic pigmentation type.

All lesion images used in the study were obtained retrospectively from photographic libraries at various institutions, and participants provided verbal or written consent for their use. Formal ethics approval for the study was obtained at the coordinating center (Sydney Melanoma Diagnostic Centre, Australia). When relevant, institutional review board approval or waiver at the individual external sites was sought.

DERMOSCOPIC FEATURES

The features included in the study were determined by consensus of the members of the International Dermoscopy Society. Before scoring, clinicians were given a morphologic tutorial to define all vascular and more recently defined structures. The definitions of the features are as described previously.[7] Twelve scorers blinded to the lesion diagnosis scored 99 indi-

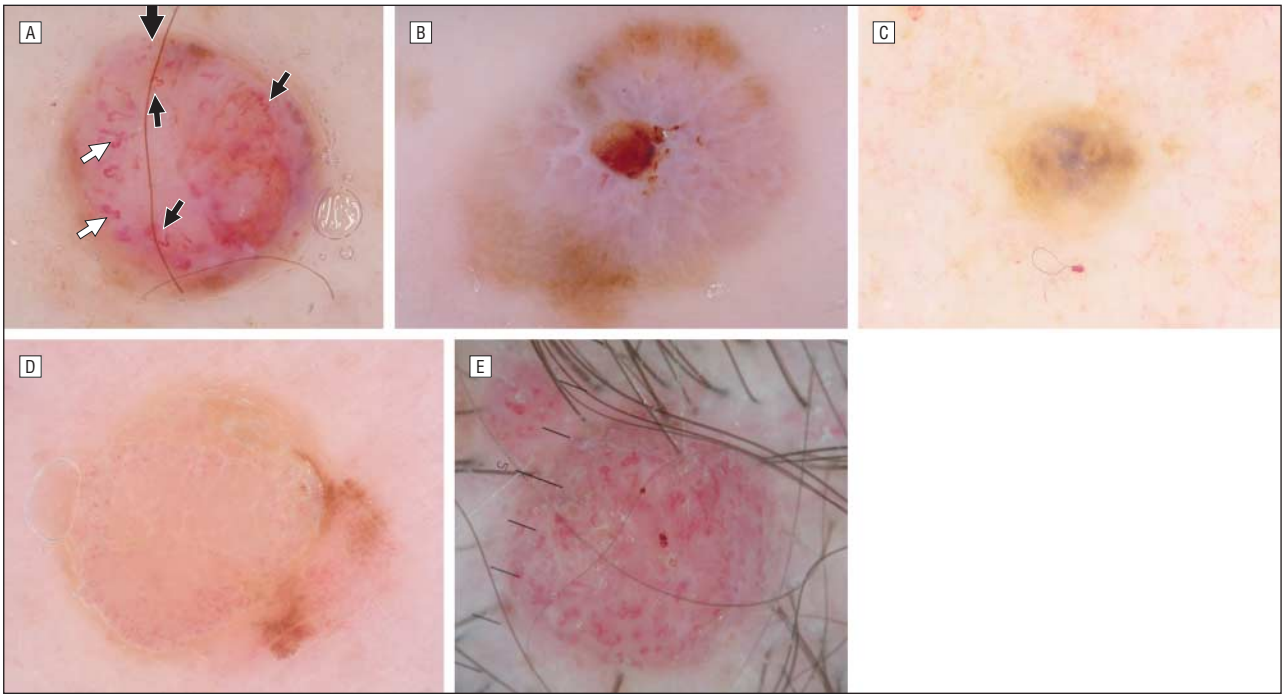

Figure 4. Amelanotic/hypomelanotic nodular melanoma (NM). A, This hypomelanotic nodule has atypical vasculature shown as combinations of dotted (thick arrow), linear irregular (thin black arrows), and hairpin vessels (white arrows) (Breslow thickness, 2.2 mm). B, This lesion has a central white patch mimicking a dermatofibroma. A total of 12.9% of amelanotic/hypomelanotic NMs were reported to have central white patches. In this case the ulceration led to a suspicion of malignancy (Breslow thickness, 2.2 mm). C, This small-diameter hypomelanotic (light-colored) nodule has asymmetrical pigmentation with areas of blue-white veil (Breslow thickness, 0.94 mm). D, This hypomelanotic lesion has fine, predominantly linear irregular vessels at the periphery of the nodule (Breslow thickness, 1.87 mm). E, This amelanotic nodule has diffuse hairpin vessels throughout the lesion in a symmetrical pattern (Breslow thickness, 2.0 mm).

ers were assigned to each method, with these scorers having varying degrees of experience with their scoring method. Hence, these results may differ if a larger group of more- or less-experienced scorers is recruited. Nevertheless, all methods tested showed a decrease in absolute sensitivity with pigmented NM compared with nonnodular invasive melanoma.

In conclusion, although there may be a bias in this study toward lesions that were suspicious and hence photographed, most pigmented and hypomelanotic NM lesions had dermoscopy features that allow their diagnosis. In the pigmented variety, the clinician needs to be aware of the small but significant number of lesions that have symmetry of pattern under dermoscopy examination. Hence, when a progressively growing, symmetrically patterned melanocytic nodule is identified, the diagnosis of NM needs to be excluded. Indeed, we believe any nodular lesion that cannot be confidently diagnosed as benign should be excised.

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Author Contributions: Dr Menzies had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. *Study concept and design*: Menzies. *Acquisition of data*: All authors. *Analysis and interpretation of data*: Menzies and Byth. *Drafting of the manuscript*: Menzies and Byth. *Critical revision of the manuscript for important intellectual content*: All authors. *Statistical analysis*: Byth and Menzies. *Obtained funding*: Menzies. *Administrative, technical, or material support*: Menzies and Avramidis. *Study supervision*: Menzies.

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