Clinical practice guidelines for the diagnosis and management of melanoma: melanomas that lack classical clinical features

Victoria J Mar1,2, Alex J Chamberlain1,2, John W Kelly1,2, William K Murray3, John F Thompson4,5

There is evidence that the rate of early detection of superficial spreading melanomas in Australia has improved, with a corresponding reduction in both the median tumour thickness and in melanoma mortality from this subtype.1 However, a number of studies in Australia and other countries have shown an increasing or stable incidence rate of thick melanomas.2-7 Nodular melanoma (NM), desmoplastic melanoma (DM) and acral lentiginous melanoma (ALM) are often diagnosed when they are much thicker lesions compared with superficial spreading melanoma (SSM).3,4,6-10 This is in part due to their atypical clinical features. Improved diagnostic accuracy of these subtypes can significantly reduce mortality from melanoma.

The 2008 evidence-based clinical practice guidelines for the management of cutaneous melanoma (http://www.cancer.org.au/content/pdf/HealthProfessionals/ClinicalGuidelines/ClinicalPracticeGuidelinesManagementofMelanoma.pdf) are currently being revised and updated in a staged process by a multidisciplinary working group under the auspices of Cancer Council Australia. This article summarises the atypical clinical features of melanoma. The new guidelines chapter containing more detailed descriptions of the clinical presentations of distinct melanoma subtypes, as well as other completed chapters of the revised guidelines, can be accessed online at http://wiki.cancer.org.au/australia/Guidelines/Melanoma.

Method

The study question “How do atypical melanomas present?” was determined by the multidisciplinary Melanoma Guidelines Working Party. To collect all relevant evidence, a literature search was performed in 2015 by the Cancer Council Australia Clinical Guidelines Network using PubMed and Embase, with the key words “atypical melanoma”, “typical melanoma”, “nodular melanoma”, “desmoplastic melanoma”, “amelanotic melanoma”, “amelanosis”, “acral lentiginous melanoma”, “subungual melanoma”, “scalp melanoma” and “clinical features”. Given the nature of the study question, a broad range of study designs including case-control, cohort and comparative studies were included in the search criteria. Information from the search was collated and summarised, and key findings that directly addressed the study question formed the main evidence summary, with level of evidence determined using the National Health and Medical Research Council evidence hierarchy (https://www.nhmrc.gov.au/_files_nhmrc/file/guidelines/developers/nhmrc_levels_grades_evidence_120423.pdf). Practice points were included based on expert consensus.

Recommendations

Melanomas may not conform to the usual ABCD (asymmetry, border irregularity, colour variegation, diameter > 6 mm) criteria. They are sometimes symmetrical, dome shaped and skin coloured (Box 1 and Box 2). A useful extension of the ABCD criteria involves adding EFG (elevated, firm and growing) criteria — any lesion that is elevated, firm and growing over a period of more than one month should raise suspicion for melanoma.11

Lack of pigment is significantly associated with poorer diagnostic accuracy.12-14 Up to 20% of all melanomas are only partially pigmented (hypomelanic), with completely amelanotic melanomas much less common.13,14 Nodular, desmoplastic and acral lentiginous subtypes are more commonly hypomelanic (over 40% of cases) compared with superficial spreading and lentigo maligna subtypes (about 10–25% of cases).13,15,16 Spitzoid melanomas are also commonly non-pigmented.17 Hypomelanic melanomas may mimic basal cell carcinomas clinically, with a slightly shiny surface and atypical vessels on dermoscopy (Box 1). Other dermoscopic clues include scar-like depigmentation, an inverse network, irregular blue-grey dots, a blue-white veil, and milky pink areas or shiny white streaks (on polarised dermoscopy only; Box 2). While dermoscopic sensitivity is about 90% for pigmented lesions, it is much lower for predominantly amelanotic lesions.

Although many NMs are seemingly non-pigmented, closer inspection reveals faint pigmentation in some and focal pigmentation in others. Dermoscopy shows melanin pigment in 90% of NMs, although 27% in one large series were lightly or focally pigmented and 9.6% were completely amelanotic.18 Compared with non-nodular subtypes, dermoscopic features such as...
blue-white veil, homogeneous blue areas, black areas, milky pink areas, atypical vessels and symmetrical (rather than asymmetrical) pigment patterns are more commonly identified.19

Dermoscopy is less useful in diagnosing DM unless features of an associated radial growth phase melanoma are present. It may be misdiagnosed clinically as a dermatofibroma, scar or non-melanoma skin cancer. Recurrence at the site of a previous biopsy diagnosed as benign on histopathology (eg, as dermatofibroma, neurofibroma, scar) is not an uncommon presentation of DM, as the histopathology can be difficult in some cases, particularly with a partial biopsy. Review of previous pathology may be helpful when there is clinical suspicion.

Over 30% of ALMs are hypomelanotic16 (Box 3 and Box 4). Occasionally, ALMs are verrucous and may mimic a plantar wart or macerated tinea infection. If an ALM were to be incorrectly diagnosed as a wart and inadvertently pared down, it would not show the typical pinpoint vessels of a wart (Box 4). Dermoscopy is helpful when the parallel ridge pattern of pigment can be identified. Hypomelanotic subungual melanoma may present as nail dystrophy and be readily mistaken for nail trauma or infection (Box 5).

Tumour thickness is not necessarily related to diagnostic delay.2,20-22 While some melanomas grow slowly over a number of years, others will become thick and life-threatening over weeks or months. More rapid growth has been associated with nodular and

---

**Guideline summary**

1 Amelanotic desmoplastic melanoma on the scalp (5.8 mm thick)

A: Shiny, symmetrical, dome-shaped scalp nodule. B: Polarised dermoscopy (magnification, ×10) demonstrates atypical polymorphic vessels (>), milky pink areas (x) and lacks the typical in-focus arborising vessels of a basal cell carcinoma.

2 Superficial spreading melanoma (0.5 mm thick) on the posterior leg

A: New and growing shiny pink plaque with focal hyperkeratosis, easily mistaken for an inflamed seborrhoeic keratosis. B: Polarised dermoscopy (magnification, ×10) demonstrates an atypical vascular pattern with both dotted vessels and red globules (> along with focal hyperkeratosis, shiny white streaks (crystalline structures) (<), milky pink structureless areas (x) and trace light brown pigment (#). Pathology revealed a 0.5 mm thick superficial spreading melanoma with 2 mitoses/mm².

3 Acral lentiginous melanoma (3.1 mm thick)

A: Large linear hyperkeratotic and focally eroded plantar plaque with faint pigment at the rim and inferior pole (easily mistaken for verruca or chronic scar). B: Subtle pigmentation is more obvious under Wood lamp examination (white dotted line).

4 Ulcerated hypomelanotic acral lentiginous melanoma (4.8 mm thick)

A: Well circumscribed pink/red nodule, which could be mistaken for a verruca; however, it does not have the typical pinpoint vessels. B: Instead, polarised dermoscopy (magnification, ×10) reveals atypical vessels (>), shiny white streaks (*) and focal pigmentation (arrow).

5 Ulcerated subungal melanoma (6 mm thick) previously mistaken for nail trauma

Melanin pigment is evident at the proximal and lateral nail folds (Hutchinson sign shown by arrows) and there is pigment in the nail bed with haemorrhage.
6 Evidence summary for atypical presentations of melanoma

<table>
<thead>
<tr>
<th>Evidence</th>
<th>NHMRC level*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nodular, acral lentiginous and desmoplastic subtypes more commonly present as thick lesions; improved diagnostic accuracy of these is therefore critical</td>
<td>III-2, III-3, IV</td>
</tr>
<tr>
<td>Nodular melanomas are associated with more rapid vertical growth compared with superficial spreading melanomas</td>
<td>III-3, IV</td>
</tr>
<tr>
<td>Up to 20% of all melanomas are amelanotic or only partially pigmented, with this being more common among nodular, acral lentiginous and desmoplastic subtypes</td>
<td>IV</td>
</tr>
<tr>
<td>Amelanosis/hypomelanosis is significantly associated with poorer diagnostic accuracy</td>
<td>III-2, III-3</td>
</tr>
</tbody>
</table>

* For details of the National Health and Medical Research Council (NHMRC) evidence hierarchy, see https://www.nhmrc.gov.au/_files_nhmrc/file/guidelines_developers/nhmrc_levels_grades_evidence_120423.pdf.

Practice points

- Melanomas are generally distinguished from benign lesions by their history of change, and thick melanomas often do not conform to the ABCD rule but usually meet the EFG criteria. Therefore, careful history taking is important, and any lesion that continues to grow or change in size, shape, colour or elevation over a period of more than one month should have a biopsy taken and be assessed histologically or referred for expert opinion.

- Suspicious raised lesions should be excised rather than monitored.

Acknowledgements: We thank Laura Wuefliner, Jutta von Dincklage and Jackie Buck from the Cancer Council Australia Clinical Guidelines Network for their assistance in this work. Development of the new Clinical Practice Guidelines for the Diagnosis and Management of Melanoma was funded by Cancer Council Australia and Melanoma Institute Australia, with additional support from the Skin Cancer College Australasia.

Competing interests: No relevant disclosures.

Provenance: Not commissioned; externally peer reviewed.

© 2017 AMPCo Pty Ltd. Produced with Elsevier B.V. All rights reserved.

References: