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Cutaneous melanoma

Atypical variants and presentations

Background

The incidence of melanoma continues to rise in Australia. General practitioners treat the majority of skin cancers affecting Australians. In the past decade, there has been improved uptake of dermoscopy by GPs who realise its value in the assessment of pigmented and nonpigmented lesions.

Objective

This article outlines those variants or presentations of melanoma that create diagnostic difficulty for all clinicians. Practice tips regarding clinical features or useful dermoscopic clues are included.

Discussion

A clinical overview of lentigo maligna, acral lentiginous and subungual melanoma, nodular melanoma, desmoplastic melanoma, verrucous melanoma and hypomelanotic melanoma is presented. Dermoscopy has become a vital diagnostic aid in the assessment of all skin lesions. Its value in the diagnosis of melanoma is highlighted where relevant. Expert dermatopathology assessment is equally as crucial in reaching a correct diagnosis, especially for some of these atypical variants.

■ **Given that the prognosis associated with cutaneous malignant melanoma is closely associated with tumour thickness, it is imperative that melanomas are diagnosed at the earliest stage possible. When melanoma is suspected, early excisional biopsy or urgent referral is the most critical management step. Readers are urged to familiarise themselves with the current national recommendations regarding biopsy techniques, appropriate excision margins, relevant investigations and appropriate follow up, which are outlined in the recently revised Australian Cancer Network *Melanoma clinical practice guidelines*.¹**

Lentigo maligna and lentigo maligna melanoma

Lentigo maligna (LM) (melanoma in situ, lentigo maligna type) and its invasive counterpart, lentigo maligna melanoma, account for 10–15% of all melanomas. While these are typically slow growing, reaching a diagnosis can be challenging on severely solar damaged skin, particularly as these variants must be distinguished from other common and benign pigmented lesions such as pigmented solar keratosis, pigmented intraepidermal carcinoma, solar lentigo, lentigo simplex, and pigmented and sessile seborrheic keratosis.

Clinically, LM is frequently ill defined and variably pigmented (*Figure 1*), and may occasionally be hypomelanotic or partially pigmented. It is sometimes known to approach or involve mucosal margins, and may cross cosmetic subunits of the face. Subclinical extension beyond apparent margins is a frequent clinical dilemma. Histologically, LM can be difficult to distinguish from the atypical melanocytes seen in solar damaged skin, and for this reason, margins can be indistinct; margin controlled surgery has been advocated for this very reason.

One Australian study of mapped serial excision for LM of the head and neck showed that a 5 mm margin on clinically involved skin was inadequate in 20% of cases of primary LM and over 50% of recurrent LM.² Partial biopsies may be nonrepresentative, but are unavoidable at times. When an excisional biopsy is impractical, a deep shave biopsy (saucerisation biopsy) usually provides adequate material for histopathological examination. These should be taken from the



most suspicious area, preferably guided by dermoscopy and sent to a dermatopathologist for reporting.¹ Where it is difficult to determine the histopathological limit of LM in solar damaged skin, a punch biopsy from the contralateral face can aid the pathologist. This enables comparison between LM and background atypical melanocytes seen in solar damage.

Good magnification and lighting, as well as Wood's light illumination (black light) aid in delineating LM before planning initial biopsy.³ Dermoscopy is also a valuable diagnostic aid, as LM has a number of unique features including asymmetric perifollicular openings and rhomboidal structures (*Figure 2*). Interfollicular peppering or 'annular granular structures' (*Figure 3*) are also useful, although these may be seen in certain solar lentigines, lichenoid or solar keratoses.⁴ All facial pigmented macules tend to show pseudonetwork so this is not a useful discriminating dermoscopic feature. Reticular network is not seen because the rete ridges on facial skin are effaced. Obliteration of follicular openings or milky pink erythema often signify the development of invasive melanoma.

Practice tips

- Biopsy is advisable for all changing facial pigmented macules
- Dermoscopy is a valuable diagnostic aid in the assessment of possible lentigo maligna
- Lentigo maligna may extend beyond the apparent clinical margins of the lesion.

Acral lentiginous and subungual melanoma

Acral lentiginous melanoma (ALM) is an uncommon variant occurring exclusively on the palms of the hands and soles of the feet. It is not thought to be related to ultraviolet (UV) exposure. It is the commonest subtype of melanoma in deeply pigmented or Asian skin, but does not occur in greater numbers in these patients than that seen in those with fair skin. Genetic profiling studies have shown that melanocyte field changes frequently extend into seemingly normal skin (both clinically and histopathologically) and this helps to understand why these melanomas recur or have skip areas of involvement⁵ (*Figure 4*).

Acral lentiginous melanoma usually presents as a sizeable pigmented macule; there is typically some delay in diagnosis. The presence of invasion can be deceptive and may be present in entirely flat lesions. Occasionally ALM masquerades as a wart, and is verrucous and nonpigmented. In large, warty lesions where there is a poor response to treatment, or where paring does not produce the typical pinpoint bleeding of a verruca, a biopsy should be taken.

Dermoscopically, the parallel ridge pattern is highly specific for melanoma, especially in situ or early invasive examples (*Figure 5*). This pattern highlights the small, round eccrine openings and is quite distinct from the other patterns associated with benignity, such as the furrow (*Figure 6*), fibrillar or lattice patterns.⁶ Occasionally globules are seen in acral naevi arranged symmetrically either side of the furrows. Application of liquid ink can help to distinguish the dermatoglyphic furrows where doubt exists, as these will stain preferentially over the ridges.⁷

Figure 1. Ill defined lentigo maligna on the left nasal tip



Figure 2. Dermoscopic image of lentigo maligna demonstrating rhomboidal structures extensive peppering and asymmetric perifollicular openings



Figure 3. Dermoscopic image of lentigo maligna melanoma demonstrating extensive annular granular structures, scar-like depigmentation and multiple colours



Melanoma of the nail matrix or subungual melanoma is considered a variant of ALM, and typically presents on the great toe or thumb, as a broad and expanding pigmented band known as 'longitudinal melanonychia' (*Figure 7*). The band arises proximally and extends to the free margin and may cause associated nail dystrophy. Adjacent nail fold pigmentation may be seen, the so-called 'Hutchinson sign'.

Dermoscopically, the band can be visualised with greater detail and can be seen as multiple lines of varying pigment, width and spacing. The parallel nature of the lines that one sees in benign subungual naevi or lentigines may be lost ('disruption of parallelism').



Blood spots are not uncommonly seen in melanoma.⁸ The major differential diagnosis for subungual melanoma is subungual haematoma, which is readily identified dermoscopically by its colour (red through blue-black), splash-like profile, and presence of blood

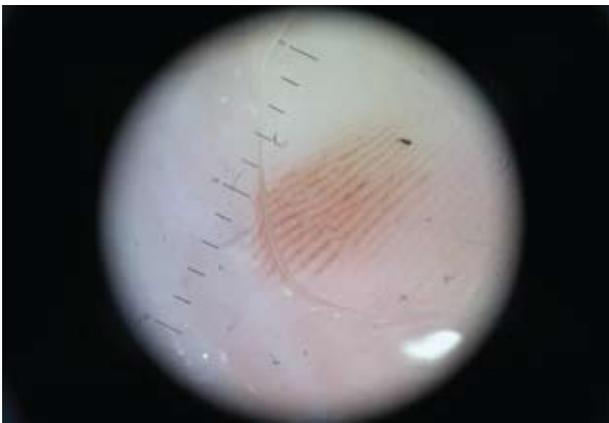
Figure 4. Extensive level IV acral lentiginous melanoma including amelanotic nodule (first cleft), patchy depigmentation and skip areas



Figure 5. Dermoscopic image of acral lentiginous melanoma seen in Figure 4, demonstrating parallel ridge pattern which highlights the eccrine openings



Figure 6. Dermoscopic image of a benign acral naevus demonstrating the parallel furrow pattern



spots. Even when deep purple or blackened in colour, a haematoma will not conform to the band-like pattern of a melanoma. These can be followed, as they will grow out over months. The ideal immersion medium for visualising nail plate or subungual pigmentation is ultrasound gel as it conforms to the undulating and irregular surface without dripping.

Practice tips

- Early acral lentiginous melanoma is readily identifiable dermoscopically by the parallel ridge pattern
- Subungual haematoma and subungual melanoma have distinct dermoscopic features, although blood spots may be seen in both
- Ultrasound gel is the ideal immersion medium for nail plate dermoscopy.

Nodular melanoma

Nodular melanoma (NM) is the second commonest subtype after superficial spreading melanoma and accounts for approximately 15% of all melanomas. It makes up the majority of thick lethal tumours⁹ and shows rapid growth, estimated at 0.49 mm depth per month.¹⁰ Nodular melanoma tend to occur on the heads and necks of elderly sun damaged men. Clinically NM are firm, symmetrical and evenly pigmented papules or nodules (Figure 8) that eventually ulcerate (Figure 9), bleed and draw the patient’s attention readily. While NM grow quickly, they don’t usually show the colour change that one associates with radial growth phase melanomas. Over 50% of NMs are predominantly hypomelanotic, and for this reason, are commonly mistaken for nonmelanoma skin cancer.¹¹ The ABCD *aide memoire* (asymmetry, border irregularity, colour variation and diameter >6 mm) for the diagnosis of melanoma applies poorly to NM. Rather, NM tend to show elevation, are firm to palpation and grow rapidly, best recalled using the EFG (elevated, firm and growing quickly) mnemonic.¹²

Dermoscopically NM usually show an atypical vascular pattern¹³ along with blue-grey veil and multiple colours. They lack features common to radial growth phase melanomas or thin melanomas such as branched streaks, pseudopods, atypical or inverse network. Regression structures are also usually absent. Some trace of pigment is usually visible dermoscopically, even in hypomelanotic tumours, and this often occurs at the margin. As a general rule, a firm papule or nodule should never be subjected to any form of monitoring – biopsy if the diagnosis is in doubt.¹⁴

Practice tips

- Nodular melanoma defy ABCD criteria but show rapid growth and mimic nonmelanoma skin cancers in appearance
- Nodular melanoma may demonstrate dermoscopic clues such as an atypical vascular pattern, marginal pigmentation, multiple colours and blue-grey veil
- Never simply monitor a nodule or raised lesion – biopsy is preferable where the diagnosis is in doubt.



Desmoplastic melanoma

Desmoplastic melanoma (DM) is a rare subtype of spindle cell melanoma that provokes a scar-like tissue reaction and is frequently associated with neurotropism. It typically affects elderly, sun damaged patients, and especially occurs on the scalp (but may occur elsewhere).¹⁵ Some cases are associated with overlying LM. They usually present as a nonpigmented, skin coloured and indurated dermal papule, plaque (Figure 10) or nodule. Most have reached significant depth at diagnosis. Desmoplastic melanoma tends to be associated with higher rates of local recurrence, and the long held belief that prognosis is better than other melanoma subtypes thickness for thickness has recently been questioned.¹⁶ This subtype of melanoma usually lacks any valuable dermoscopic features.¹⁷

Practice tips

- Consider desmoplastic melanoma when assessing scar-like plaques without a specific history of trauma
- Dermoscopy is less useful in the diagnosis of desmoplastic melanoma.

Figure 7. Subungual melanoma in situ of the great toe – a broad and multicoloured pigmented band is seen (longitudinal melanonychia)



Figure 8. Amelanotic nodular melanoma



Verrucous melanoma

Rarely, melanoma may be warty and papillomatous and mimic either a verruca, seborrhoeic keratosis, or a compound or congenital naevus. These lesions tend to be large and occur on the backs and limbs of men aged over 50 years (Figure 11).

Histopathologically they also pose a diagnostic challenge because of the naevoid features and exophytic papilliferous growth pattern.¹⁸

Practice tip

- All large warty and pigmented plaques changing over time deserve close clinical and dermoscopic assessment.

Hypomelanotic and regressed melanoma

Not all melanomas are blackened, and studies to date probably underestimate the incidence of hypomelanotic melanoma (HM). It is the authors' experience that up to 20% of all melanomas are hypomelanotic or only partially pigmented.¹⁹ Nodular melanomas are not the only subtype that is frequently hypomelanotic – DM and ALM may also be only partially pigmented in over 40% of

Figure 9. Ulcerated nodular melanoma



Figure 10. Desmoplastic melanoma





cases.¹⁹ The figure for superficial spreading and LM is closer to 10–20%. Truly amelanotic or completely nonpigmented melanoma is much rarer. The exact reason why some melanomas are hypomelanotic remains obscure, but may relate to abnormal melanogenesis or loss of functional capacity on behalf of rapidly proliferating tumour cells.²⁰

Figure 11. Verrucous melanoma

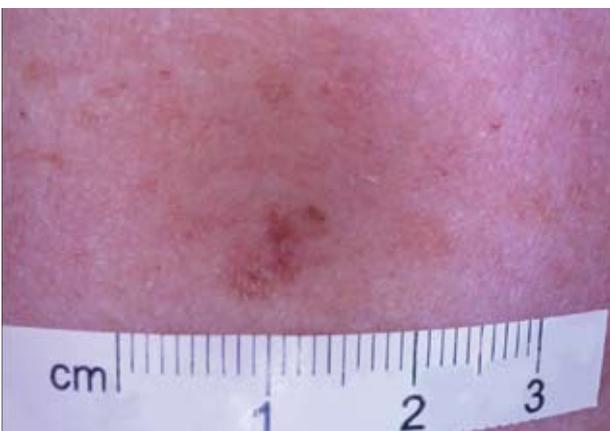


Photo courtesy: Dr Martin Haskett and MoleMap

Figure 12. Hypomelanotic superficial spreading melanoma



Figure 13. Eczema-like hypomelanotic level 1 superficial spreading melanoma



Hypomelanotic melanoma presents in a number of ways – a pink nodule, a scar-like plaque (Figure 12), a pseudo-inflammatory plaque (Figure 13), or as an extensively regressed lesion (Figure 14). The differential diagnosis for a pink patch, plaque or nodule is long, and obviously includes other nonmelanoma skin cancers. Hypomelanotic melanoma is ultimately a diagnosis of exclusion and diagnosis is frequently delayed. It should be always considered when a lesion is changing or shows any pigmentation, especially marginal, or where there is some clinicodermoscopic discordance.²¹ Ablative therapies such as cryotherapy or laser should only be used on pink lesions where there is a confident diagnosis, ideally histopathology. When HM are treated in this way, they usually recur, thereby delaying diagnosis – this is a pitfall best avoided.²²

Dermoscopic clues to HM include:

- variable pigment network or structures (including brown globules)
- inverse network
- atypical vasculature
- milky red or pink veil
- milky red, blue-grey dots and regression structures (peppering with scar-like hypopigmentation) (Figure 15, 16).

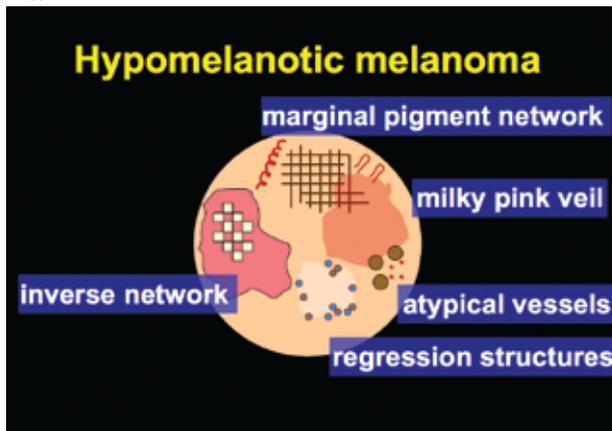
Figure 14. Extensively regressed melanoma



Figure 15. Dermoscopic image of 0.4 mm level II hypomelanotic melanoma, demonstrating regression structures, typical and inverse pigment network and milky pink erythema



Figure 16. Schematic image of dermoscopic features of hypomelanotic melanoma



It is important to remember that dotted vessels on dermoscopy are listed as a melanocytic criterion.²³ Hypomelanotic melanomas often display a range of vessels which become longer and more tortuous with Breslow depth. In a recent study of hypomelanotic melanoma, blue-grey veil was shown to be the most significant predictive dermoscopic feature. Multiple colours and centrally located vasculature (both linear irregular and/or dotted vessels) were also significant predictors.²⁴

Regression is primarily a histopathological term used to describe the inflammatory infiltrate and fibrosis seen commonly in melanoma as a host response. Clinically this manifests as partial clearance of the melanoma and dermoscopically one sees peppering or multiple blue-grey dots surrounding scar-like hypopigmentation. Any pigmented lesion showing partial clearing (*Figure 14*) or extensive, asymmetric or peripherally based peppering (*Figure 15, 16*) should be considered suspicious.²⁵

Practice tips

- Always consider melanoma as a possible diagnosis when evaluating any changing red or pink lesions, particularly where there is pigment
- Use gentle pressure to see the pigment dermoscopically (this will 'bleach' the vascular blush)
- Rub the lesion and release the pressure to visualise the vessels
- Extensive, asymmetric or peripherally based peppering or granularity within a pigmented lesion is a possible pointer to melanoma.

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