Michael Tran, Li-Chuen Wong, Vallapan Thiruvilangam and Denis Moir

Atypical melanoma:

clinicopathological features and management in general practice

M Tran (ORCID: 0000-0001-7530-8462), BSc(Med)Hons, FRACGP, AFHEA, DCH, GP, Church St Medical Practice, Newtown, NSW; lecturer, University of New South Wales, Sydney; conjoint lecturer, Western Sydney University, Sydney. **L-C Wong** (ORCID: 0000-0001-7819-6603), MBBS (Hons), MM, FACD, DCH, head of dermatology department, Children's Hospital, Westmead; clinical senior lecturer, University of Sydney, Sydney; chair, NSW Faculty, Australasian College of Dermatologists. **V Thiruvilangam** (ORCID: 0000-0001-5510-194X), MBBS, MD, FRCPA, DipPath, anatomical pathologist; **D Moir** (ORCID: 0000-0003-1288-0749), MBBS, IFCAP, GMQ, FRCPA, anatomical pathologist, Douglass Hanly Moir Pathology, NSW.

Address for correspondence

Michael Tran, 280 Church St, Newtown, NSW, Australia, 2042.

Email: Michael.m.tran@unsw.edu.au

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ATYPICAL MELANOMA

Melanoma is a significant cause of morbidity and mortality. It is the fifth most common cancer in the UK, accounting for 4% of all cancer cases.[1] There are approximately 16 700 cases identified in the UK each year, with 2300 deaths. It is estimated that atypical and hypomelanotic melanomas may account for up to 20% of all melanomas.[2] Confusion of amelanotic melanomas with other benign lesions often leads to diagnostic delay and worse prognosis.

ROLE OF GENERAL PRACTICE IN MELANOMA DIAGNOSIS

GPs are at the frontline of melanoma diagnosis and need to be aware of different clinical presentations and common mimics. Detection of melanoma at an earlier stage of disease heralds a better prognosis. The rate of early detection of superficial spreading melanomas has improved, with a reduction in the median tumour thickness and in melanoma mortality.[3] There is, however, a stable to increased rate of thick melanomas. Subtypes including nodular melanoma, desmoplastic melanoma, and acral lentiginous melanoma are often diagnosed when thicker, in part because of their atypical features.[2] Improving the diagnostic rates of unusual presentations of melanoma, which remain a diagnostic challenge, can reduce mortality.

CLINICAL VIGNETTE

A woman, aged 39 years with Fitzpatrick type 1 skin, presented with a 1-year history of an evolving, oval-shaped, pale macule over her right forearm. It measures 1 cm × 1 cm, becoming gradually more hypopigmented compared with surrounding skin (Figure 1). Central telangiectasia was seen on dermatoscopy. The lesion was non-tender, with no associated pruritus or discharge. There were no similar lesions elsewhere.

SALIENT CLINICAL FEATURES OF ATYPICAL AND AMELANOTIC MELANOMAS

Atypical melanomas may not conform to the commonly used ABCD (asymmetry, border irregularity, colour variegation, diameter >6 mm) criteria of suspicious lesions. They can be symmetrical, dome shaped, skin coloured, and unchanging. A lack of pigment may be falsely reassuring to clinicians. A useful extension of this criteria is the addition of EFG (elevated, firm, and growing). A high index of suspicion is warranted if any of the EFG criteria are present and persistent, even if a benign mimic is considered (Table 1).[4]

Table 1. Common differential diagnoses of amelanotic melanoma

Lesion type	Clinical features
Basal cell cancer	Slowly growing plaque or nodule, often skin coloured with spontaneous bleeding and ulceration
Spitz naevus	Often found in children and young adults — dome-shaped erythematous papule on the face or limbs. May be pigmented
Seborrhoeic keratosis	Highly variable appearance including papules and plaques, mixed colours, and smooth, waxy, or warty texture
Actinic keratosis	Thickened papule or plaque, sometimes scaly or horny, white/red/skin-coloured lesion in sun-exposed regions
Dermatofibroma	Solitary, firm papule or nodule on a limb with colours variable from pink to dark brown
Pyogenic granuloma	Fleshy red nodule, often rapidly developing and prone to bleeding

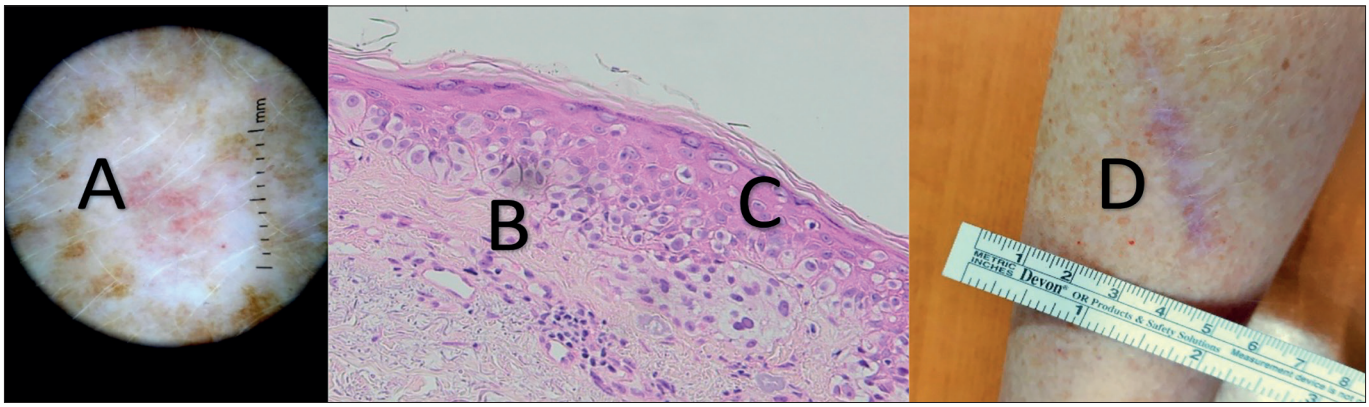

Figure 1. Dermatoscopic image of atypical melanoma showing hypopigmented 'halo' with central blush (A). Excision required 2 cm margins and primary closure (D). The same lesion at × 200 magnification on histology showing proliferation of melanocytes with nuclear atypia along the basal layer (B) with pagetoid spread to the granular layer (C).

Lesion change is an important assessment criterion and may be detected by the patient[3] or on serial clinical review and imaging. Some changing lesions will prove benign, however, and a slowly changing melanoma may not appear to be clinically different. Other risk factors include increasing age, cumulative UV exposure, fair skin and hair (though acral lentiginous melanomas are more common in those of African or Asian descent), multiple naevi, a strong family history, and comorbidities including inflammatory bowel disease and immunocompromise.[5]

DERMOSCOPIC FEATURES PRESENT IN ATYPICAL AND AMELANOTIC MELANOMAS

Dermoscopic clues in atypical melanomas include a shiny surface, atypical and polymorphous vessels, scar-like depigmentation, an inverse network, irregular blue-grey dots, a blue-white veil, milky pink areas, and shiny white streaks. Close inspection of seemingly amelanotic lesions may reveal faint widespread or focal pigmentation. Dermoscopic sensitivity, quoted at 90% for pigmented lesions, is lower for amelanotic or partially pigmented lesions,[2] where there is poorer diagnostic accuracy. Nodular, desmoplastic, and acral lentiginous subtypes are more commonly hypomelanotic (>40% of cases) when compared with superficial spreading and lentigo maligna subtypes.[2]

IMPORTANT HISTOPATHOLOGICAL FEATURES OF ATYPICAL MELANOMAS

The melanomas that are considered atypical clinically may be either typical or atypical on histology. Atypical presentations can be due to variable lack of melanin in a lesion without junctional cellular activity, or because of the lesion mimicking another non-melanocytic cutaneous entity. Though there are often a lack of melanin granules in the melanocytes in an atypical melanoma (Figure 1), visible melanin is seen in 5%, with increased detection when melanin-specific stains (such as SOX-10, S100, Melan A, HMB45, MITF, and PRAME) are performed.[6] Thorough analysis with close clinical, histological, and immunohistochemical correlation are required to diagnose melanoma or one of its mimics.[7]

RECOMMENDED INVESTIGATIONS AND MANAGEMENT FOR MELANOMA

The management of atypical melanomas is the same as for melanoma. Monitoring with sequential total body skin examinations including lymph node palpation, total body photography, and dermoscopic imaging where available provides a baseline in high-risk individuals and reduces the number of benign excisions.

Initially, a complete excisional biopsy of a suspicious lesion with 2 mm margins is the safest approach, preceding wider local excision if this is then required.[8] Partial biopsy may be considered for suspicious lesions in difficult sites or for larger lesions where closure would be difficult. The diagnostic biopsy both diagnoses and stages melanomas by providing an accurate assessment of depth and other histological features. T-staging (based on tumour thickness and ulceration) helps plan definitive management.[5] The case presented, a stage I melanoma, required excision with 2 cm margins (Figure 1).

Sentinel node biopsy is a sensitive method for detecting microscopic nodal disease at diagnosis and should be considered where risk of lymph node involvement is greater than 5% (melanomas >1 mm thick or 0.8–1 mm thick with ulceration).[8]

Definitive treatment is dependent on stage of melanoma, with excision and increasing margin size being suitable for stage 0 to stage II melanoma. Use of imiquimod, lymph node dissection, radiotherapy, systemic

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anti-cancer therapy, immunotherapy, and electrochemotherapy will depend on both stage of disease and patient factors, with specialist input recommended.[5]

RECOMMENDED FOLLOW-UP FOR MELANOMA

Follow-up after melanoma treatment aims to detect recurrent melanoma and consists of routine regular skin examinations, dermatoscopy, and photography. The frequency and duration of checks are determined by stage of disease at diagnosis.[5]

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Patient consent

The patient gave consent for publication of this article and its images.

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