Melanoma

Robert Micieli BSc, Kucy Pon MD

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1 Sun exposure plays an important role in melanoma pathogenesis

More than 90% of melanomas in the 3 most common genetic subtypes (*BRAF*, *RAS*, *NF1*) have a substantial ultraviolet signature.[1] Clinically, melanomas most commonly appear on sites of chronic (i.e., face, neck) or intermittent sun exposure (i.e., trunk, legs) as superficial spreading (Figure 1), nodular or lentigo maligna melanoma (Appendix 1, available at www.cmaj.ca/lookup/suppl/doi:10.1503/cmaj.181500/-/DC1).

2 Melanomas also occur on sites of minimal sun exposure

Genome sequencing of acral (on palms and soles) and mucosal melanomas has shown that although sun exposure may play a role, it is not the primary mutational driver.[2] These melanomas may share a pathogenesis similar to that of other noncutaneous malignancies.

3 The mitogen-activated protein kinase pathway is implicated in almost all melanomas

This pathway stimulates cell growth and survival. *BRAF*, *RAS* and *NF1* mutations are part of this pathway and represent 50%, 25% and 15% of all melanomas, respectively.[1] Genome-wide studies have helped identify important immunohistochemistry markers for diagnosis (e.g., anti–programmed cell death 1 [anti–PD-1], anti–cytotoxic T-lymphocyte-associated protein 4 [anti–CTLA4])[3] as well as adjuvant immunotherapies and targeted therapies (i.e., *BRAF* or *MEK* inhibitors) to improve survival of patients with advanced melanoma.[4]

4 Of all melanomas, 10% are amelanotic or hypopigmented and may be diagnostically challenging[5]

They are most common in patients with Fitzpatrick type I skin and chronic sun damage (actinic keratoses), and are located on sun-exposed sites (e.g., face, neck, upper arms, hands).[5] The differential diagnosis for evolving red or pink macules, plaques or nodules should include amelanotic melanoma, especially in the aforementioned patients and locations. KIT, a tyrosine kinase inhibitor, is frequently mutated in amelanotic melanoma.

5 Any lesions suspicious for melanoma should be referred to dermatology

A pigmented lesion with any of the ABCDE criteria (Figure 1) should raise suspicion for melanoma. Wide, local excision with appropriate margins is the definitive treatment. In cosmetically sensitive areas (e.g., face), Moh surgery, in which thin layers of the tumour are sequentially removed until only cancer-free tissue remains, may be preferred.

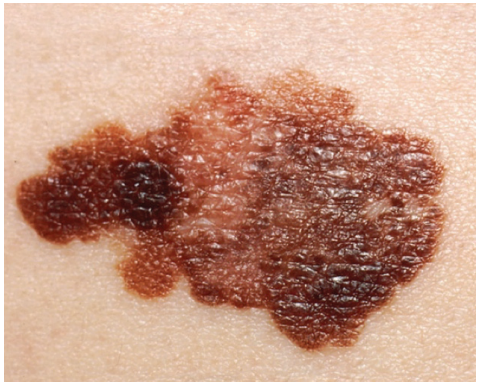

Figure 1: ABCDE criteria (Asymmetric shape, irregular Border, Colour variation, Diameter > 6 mm [about the size of a pencil eraser] and Evolution [noted on history and when compared with previous size]) of a typical superficial spreading melanoma, characterized as a plaque with flat and raised areas. Image obtained from the National Cancer Institute.

References

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Affiliations: Faculty of Medicine (Micieli, Pon), University of Toronto; Division of Dermatology, Sunnybrook Health Sciences Centre (Pon), Toronto, Ont.

Correspondence to: Kucy Pon, kucy.pon@sunnybrook.ca