Lentigo Maligna, Macules of the Face, and Lesions on Sun-Damaged Skin

Confocal Makes the Difference

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KEYWORDS

• Lentigo maligna • Melanoma • Benign facial macules • Solar damage • Confocal microscopy

KEY POINTS

- Lentigo maligna (LM) and lentigo maligna melanoma (LMM) often resemble one another and are difficult to distinguish from solar-induced macules of the face, clinically, and on dermoscopy and histopathology.
- LM/LMM has the highest recurrence rate of all melanoma subtypes despite treatment, reflecting the diagnostic and treatment ambiguities this lesion presents.
- In vivo reflectance confocal microscopy addresses many of the complexities and challenges of LM/LMM, enhancing patient care at all stages of diagnosis and management.

INTRODUCTION

Lentigo maligna (LM) is defined as a form of melanoma in situ that presents as a slowly growing variably pigmented macule typically on the sun-damaged skin of the elderly, most commonly on the head and neck.[1] LM involves the proliferation of atypical malignant melanocytes along the basal layer of the epidermis. Lentigo maligna melanoma (LMM) is defined as the invasive progression of LM, whereby atypical melanocytes are no longer confined to the epidermis.[2]

The incidence of LM is estimated to be approximately 13.7 per 100,000 person-years but is difficult to confirm due to incomplete data collection for in situ melanoma in most cancer registries.[3] Evidence suggests that LM/LMM is underestimated, and LM rates are likely to increase with an aging population in most high-income countries.[3–5] Although LM grows slowly, once invasive, it has the same prognosis as other malignant melanoma in terms of metastatic potential, when adjusted for Breslow thickness.[6]

Due to shared aetiology of UV exposure and age, LM typically copresents with general solar and aged-induced macules and lesions, which include solar lentigines (SL), pigmented actinic keratosis (PAK), seborrheic keratosis (SK), lichen planus-like keratosis (LPLK), as well as freckles and generalized UV-induced pigmentation.[7] The borders of LM are frequently obscured by their collision with these lesions and emergence on photo-damaged skin.

Distinguishing melanocytic hyperplasia in actinically damaged skin from atypical melanocytes, especially in the peripheries of LM, is difficult on histopathology.[8] There is significant controversy

Conflicts of Interest: None.

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about what constitutes a negative margin.[7,8] This controversy is reflected in high discordance rates between pathologists in interpreting excision margins.[9,10] The high recurrence rate of LM after conventional surgery, estimated to be between 8% and 31%, indicates more accurate margin assessment is needed.[11–13]

Dermoscopy has made significant progress in distinguishing LM/LMM from benign pigmented macules of the face.[14,15] Schiffner and colleagues[16] demonstrated the 4 main dermatoscopic criteria enabling 93% of lesions to be correctly identified as LM (sensitivity of 89% and specificity of 96%), while the vascular features on dermoscopy added by Pralong and colleagues[17] are particularly beneficial in assessing amelanotic LM/LMM peripheries, devoid of pigment.

There are several other studies producing dermatoscopic criteria against which the ability to distinguish LM from pigmented macules of the face are tested.[18–22] However, dermoscopy is limited by the overlap of features between benign and malignant lesions.[23,24] For example, the dermatoscopic features including gray color, gray circles, and annular granular structures can be seen in PAK and LM. Similarly, the hyperpigmented rim of follicular openings of LM/LMM can be mistaken for pseudofollicular openings of SK.[19]

There are multiple controversial issues with the time line of the disease and its progression from benign solar damage to fully invasive LMM. Early LM is extremely subtle and may involve a gradual increase in the number of individual melanocytes at the dermoepidermal junction (DEJ). Some atypical cells may be present. However, these features are also seen in severely sun-damaged skin.[8] Reflectance confocal microscopy (RCM) is well suited to assessing the morphology and subtle or complex features of a macule such as LM. It also enables the visualization of cellular features that differentiate LM/LMM from its pigmented counterparts.[25,26] RCM generates a horizontal (enface) view of at least 8 × 8 mm from stratum corneum to the level of the upper dermis at cellular resolution, an approximate depth of 250 μm, which is appropriate for assessing the radial spread of LM throughout the epidermis, often over very large areas.

CONFOCAL MAKES THE DIFFERENCE THROUGH SEVERAL APPLICATIONS

Differentiating Lentigo Maligna from Benign Macules of the Face and Solar Damage

It is important to differentiate LM/LMM from benign macules and solar damage. Diagnostic ambiguities can lead to unnecessary excisions of LM-like benign macules, which can carry surgical morbidly in the elderly patient and cosmetic issues on sensitive areas of the face.[18] Similarly, erroneous diagnosis of LM as a benign macule can lead to inappropriate management and delayed melanoma diagnosis.[27]

There are numerous case series examining the RCM features of benign lesions and solar damage in correlation with histopathology and/or dermoscopy, including the following:

- SK[25,28–32] (**Fig. 1**)
- Actinic keratosis (AK)[18,32–37] (**Fig. 2**)
- SL[27,38–40] (**Fig. 3**)
- LPLK[41]
- Chronic UV-induced changes[42–45] (**Fig. 4**)

Similarly, the features of LM/LMM have been elucidated on RCM[11,27,46–50] (**Fig. 5**). The proliferation of atypical melanocytes at the DEJ may be visualized on RCM as atypical pleomorphic cells,

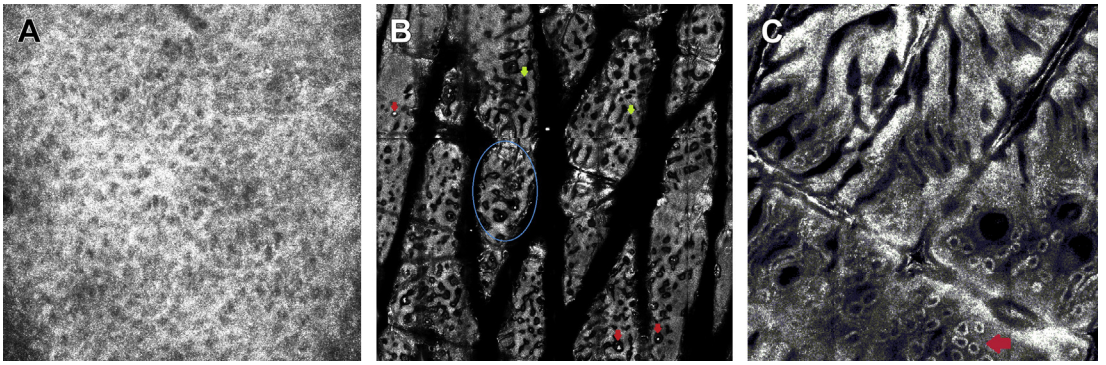

Fig. 1. Seborrheic keratosis. (*A*) Confocal image, 0.5 × 0.5 mm, of a SK with broadened honeycomb pattern in the epidermis. (*B*) Confocal images in a 4 × 4-mm mosaic of a SK in the epidermis showing cysts (*red arrows*), crypts (*green arrows*), and bulbous projections (*circle*). (*C*) Confocal images in a 2 × 2-mm mosaic of a SK in the DEJ showing a ringed pattern (*red arrow*).