Dermatology Practical & Conceptual

Toward a New Classification of Lentigo Maligna: Easy and Difficult to Treat Lentigo Maligna

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Lentigo maligna (LM) is defined as a melanoma in situ that typically develops on chronically sun-damaged skin, particularly on the head and neck. It often presents as an asymptomatic, slow growing, irregularly pigmented macule in adults over age 40 [1]. LM shows a variable long radial growth pattern with the potential to progress to invasive lentigo maligna melanoma (LMM), with an annual progression risk of approximately 3.5% [2].

Chronic ultraviolet (UV) radiation exposure is considered the main cause, explaining the frequent coexistence of LM with solar lentigines, actinic keratoses, and wrinkles in older patients [1]. Nevertheless, previous studies have revealed that LM may also appear in younger individuals as solitary heavily pigmented macule on the skin without signs of sun damage [3-4]. Moreover, sex-related differences have been also described: in females, LM often affects the cheeks, while in males, it more frequently involves the distal nose. Such clinical patterns, together with lesion size and border definition, influence treatment strategies [1,3].

Toward a New Treatment Classification of Lentigo Maligna Subtypes

Based on our clinical experience and the current literature, it can be assumed that there are at least two different types of LM:

1. Easy-to-treat LM: it arises in younger individuals as relatively small solitary, heavily pigmented and well-defined macule on otherwise normal skin (Figure 1). It is our experience that this subtype does not possess any surgical difficulty as free margins are easily achieved, with very low recurrence rate.

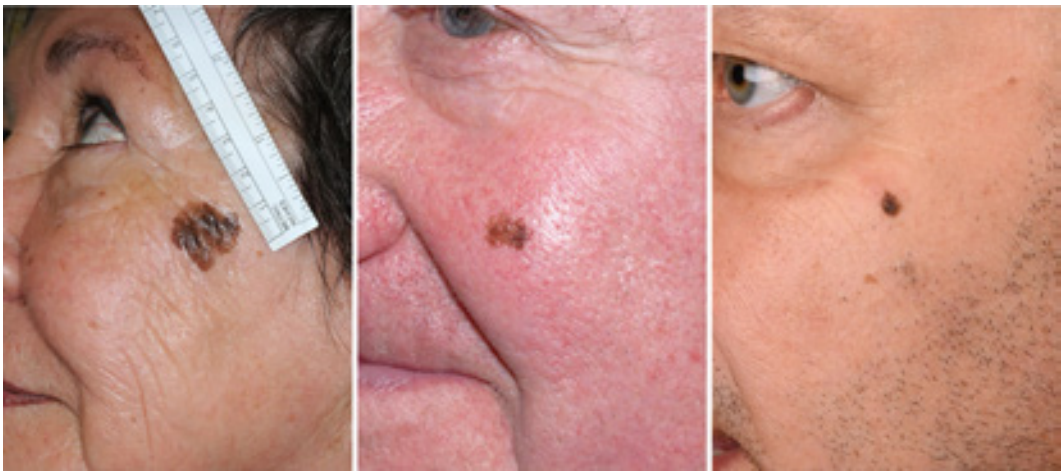

Figure 1. Examples of easy-to-treat lentigo maligna, presenting as solitary macule with well-defined borders on otherwise normal skin.

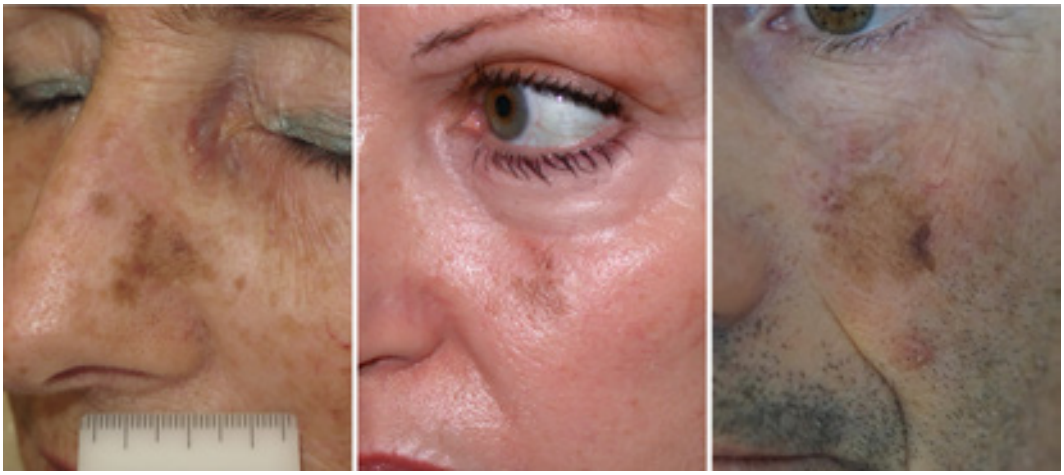

Figure 2. Examples of difficult-to-treat lentigo maligna presenting as a large, diffuse variably pigmented lesion with ill-defined borders on freckled skin.

2. Difficult-to-treat LM: it occurs more commonly in older individuals or in those with a freckled phenotype. This type presents as a larger, poorly demarcated, often irregularly light brown pigmented macule on skin with clinical signs of actinic damage (i.e., freckles, wrinkles, actinic keratoses) (Figure 2). As clinical margins are difficult to assess, and based on current literature, this subtype appears to be linked with a higher rate of incomplete excision rate or recurrence even after wide local excision (WLE). This is likely due to its subclinical extension, or presence of atypical melanocytes in the whole field (concept of field changes) [5].

The above clinical features indicate therefore the risk of recurrence of LM after surgery.

Lesion size and excision technique are major determinants of recurrence. Although 0.5 cm margins are standard, large, ill-defined lesions are often incompletely excised. A multivariate analysis showed that each 50 mm² increase in lesion area increased recurrence risk by 9% [6]. Easy-to-treat LM therefore carries a low risk, while difficult-to-treat LM carries a high risk, often in cosmetically sensitive areas.

According to this evidence, easy-to-treat LM may be regarded as a melanoma with a low risk of recurrence, due to its smaller size and clear demarcation, which facilitate complete surgical removal. On the other hand, difficult-to-treat LM can be considered melanoma with high risk of recurrence, given its size, indistinct or subclinical margins, and frequent localization to anatomically or cosmetically sensitive areas of the head and neck, where achieving clear margins can be particularly challenging. We propose to use topical imiquimod for this type of LM, either in a neoadjuvant or adjuvant setting, in order to address also subclinical disease.

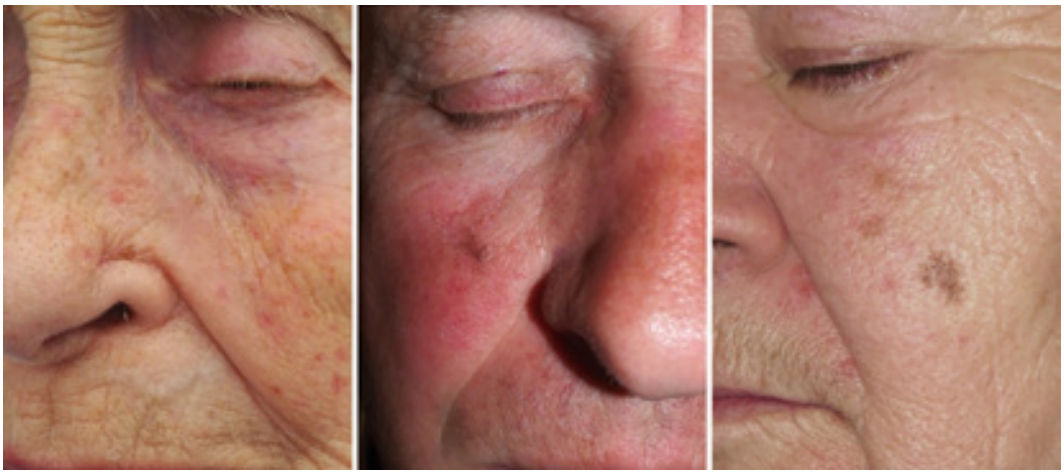

Figure 3. Examples of easy-to-treat lentigo maligna associated with rosacea.

Novel Insights into the Pathogenesis of Lentigo Maligna

The proposed dichotomy of LM into two clinical types also supports the hypothesis that they differ in terms of pathogenesis, growth behavior, and therapeutic responsiveness. In particular, difficult-to-treat LM may result from cumulative UV-induced genetic damage in epidermal melanocytes. Its high recurrence risk may not only be associated with persisting abnormal melanocytes after R1/2 resection but due to a general increase in atypical melanocytes in the whole area (similar to field cancerization in actinic keratoses) [7].

In contrast, chronic sun damage does not appear to play a major role in the development of easy-to-treat LM. In fact, this type usually affects persons without evident signs of sun damage. In this context it appears intriguing to notice that upcoming evidence suggests that chronic inflammation such as rosacea may play a role in inducing genetic mutations and molecular alterations capable of disrupting skin homeostasis, ultimately leading to dysregulated melanogenesis [8]. In a previous study we demonstrated some interesting differences with regard to the predominant subsite of LM (cheeks in females and nose in males) [3]. Notably also, rosacea reveals such sex-related differences involving mainly cheeks and front in females and nose and chin in males.

This possible pathogenetic link between the development of easy-to-treat LM and rosacea is further supported by dermoscopic findings, which have not yet been studied in detail; in many cases, LM lesions in these regions are surrounded by vessels arranged in a polygonal arrangement, a hallmark vascular pattern of rosacea. However, additional studies are necessary to explore potential genetic and inflammatory mechanisms underlying this association (Figure 3).

Therapeutic Implications

If our preliminary observation proves to be true, surgical excision remains the mainstay in the treatment of easy-to-treat LM with a low risk of recurrence and difficult-to-treat LM. However, in the latter, neoadjuvant or adjuvant treatment approaches, in particular the use of imiquimod, may reduce incomplete margins or risk of recurrence. In fact, there is already mounting evidence supporting the benefits of imiquimod for LM, although its precise role in our supposed setting remains to be further studied [1,5,9].

Conclusions

Our observations suggest that easy-to-treat LM, typically occurring in younger individuals and with a low risk of recurrence after surgery, may be linked to chronic inflammatory conditions such as rosacea. In contrast, difficult-to-treat LM, usually observed in older patients and associated with a higher risk of surgical recurrence, is more likely to develop in the context of field cancerization driven by chronic cumulative UV damage. Recognizing these distinct clinical settings may help refine diagnostic assessment and guide individualized therapeutic strategies.

Ethics Statement: The patients in this study have given written informed consent to the publication of their case details

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