Research letter

Nine per cent of biopsy-proven lentigo maligna lesions are reclassified as lentigo maligna melanoma after surgery

DOI: 10.1111/bjd.17714

Dear Editor, Lentigo maligna (LM) is a melanoma *in situ*, and its incidence is still rising in the Netherlands.[1] LM is located mostly in the face, and therefore radical surgical removal, which is the first choice of treatment, can be challenging in this delicate anatomical region. Staged excision is considered a useful alternative. The initial diagnosis of clinically suspicious LM is usually based on just one or a few biopsies, which may lead to reclassification into lentigo maligna melanoma (LMM) based on histological evaluation of the excision specimen. Due to the patients' usual age and LM localization, nonsurgical treatments such as topical imiquimod[2] – combined with laser ablation,[3] radiotherapy or careful clinical follow-up – are sometimes considered. The results of these treatments are uncertain. Many studies mention clinical clearance with response rates up to 74% with topical imiquimod.[2] One recent study showed histologically proven complete clearance after topical imiquimod in only 37% of cases.[4] When these nonsurgical treatments are considered, the fact that LMM can be underestimated based on initial biopsy must be taken into account.

The aim of our study was to calculate the proportion of biopsy-proven LMs that were upstaged to LMM after histological evaluation of the excision specimen. Moreover, we have tested the accuracy of the current pathology protocol.

All patients with histologically proven LM or LMM who were diagnosed at our centre during the period January 2010 to February 2017 were selected. Information on sex, age, size and anatomical location of the lesion, diagnostics before treatment (punch or incisional biopsy) and treatment method (including the number of excision rounds in case of staged excision) was retrieved from the clinical files. The histopathological diagnoses (LM or LMM) before and after treatment were compared.

In addition, we tested our current protocol in 25 cases with LM diagnosis based on staged excision. These patients were randomly chosen for additional histopathological evaluation. The tissue blocks (formalin fixed, paraffin embedded) with LM were selected based on the corresponding haematoxylin and eosin slides. Each block containing LM was cut for three additional (deeper) levels to exclude possible invasion (i.e. LMM). SPSS statistics 24 was used for the data analyses (IBM, Armonk, NY, U.S.A.).

In the study period, 417 patients were diagnosed with histologically proven LM or LMM at the Erasmus Medical Center. In 284 of 417 patients (68·1%) the initial biopsy showed LM, and 59 of 417 (14·1%) showed LMM (results not shown). In the first group, 28 of 284 patients (9·9%) were treated not surgically but with topical imiquimod and laser. One patient was excluded because the final diagnosis was melanoma *in situ* (results not shown). Of the remaining patients, in 232 of 255 (91·0%) the diagnosis of LM was confirmed after excision (staged or conventional), and in 23 of 255 (9·0%) the LM was reclassified as LMM or melanoma (Table 1). In the LM group 138 of 232 patients (59·5%) were female, and in the LMM

Table 1 Characteristics of patients diagnosed with lentigo maligna (LM) or lentigo maligna melanoma (LMM) between 2010 and February 2017 at the Erasmus Medical Center

Biopsy-proven LM treated with surgery (n = 255)	LM after surgery (n = 232, 91·0%)	LMM/melanoma after surgery (n = 23, 9·0%)
Male, n (%)	94 (40·5)	14 (61)
Female, n (%)	138 (59·5)	9 (39)
Age (years), mean; median	71·1; 72	73·4; 73
Size category, n (%)		
1 (< 1 cm)	44 (19·0)	3 (13)
2 (1–2 cm)	83 (35·8)	12 (52)
3 (2–5 cm)	47 (20·3)	2 (9)
4 (> 5 cm)	6 (2·6)	1 (4)
Unknown	52 (22·4)	5 (22)
Anatomical location, n (%)		
Head and neck	201 (86·6)	18 (78)
Extremities	17 (7·3)	2 (9)
Trunk	14 (6·0)	3 (13)

group nine of 23 (39%). At the time of diagnosis the mean ages of patients in the LM and LMM groups were 71 and 73 years, respectively. The LMs and LMMs were located mainly in the head and neck region (respectively 86·6% and 78%) and had an average size of 1–2 cm (Table 1). In the 25 cases of LM that were used to test the current protocol we did not find invasive melanoma after additional histopathological evaluation.

This study shows that 9% of biopsy-proven LMs turned out to be LMM after complete excision (staged or conventional). A previous epidemiological publication showed a cumulative risk of LMM of 2–3% in patients with LM (histologically confirmed) after 25 years of follow-up.[1] If there is a clinical suspicion of LM, current guidelines advise sampling with (punch or incisional) biopsy, or for small lesions complete excision.[5,6] Surgical excision is the first choice of treatment.[5,6] The current study adds that a biopsy alone may lead to underestimation of LMM. A similar finding was reported before in a group of 46 patients in whom an upgrade of 20% of LMs or melanomas *in situ* to invasive melanoma was found.[7]

For melanoma *in situ* one study reported that 33% were reclassified as invasive melanoma after additional histopathological evaluation of deeper sections.[8] We could not confirm this for LM in the 25 cases that we investigated.

In conclusion, there is a relatively high proportion (9%) of biopsy-proven LMs that are reclassified to LMM or melanoma after complete removal (either staged excision or conventional excision). This should be taken into account in the therapeutic decision making of LM. Additional histopathological evaluation of the staged excision specimens does not contribute to higher detection rates of LMM and is therefore not of added value to the current protocol.

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Funding sources: none.

Conflicts of interest: none to declare.