Mapped Serial Excision for Periocular Lentigo Maligna and Lentigo Maligna Melanoma

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Purpose: To report the early cure rate for periocular lentigo maligna (LM) and LM melanoma (LMM), using modified Mohs surgery with vertically cut paraffin-embedded sections (mapped serial excision [MSE]). A secondary aim was to identify differences in the clinical features and outcomes between periocular LM and LMM and those found elsewhere on the head and neck.

Design: Prospective, noncomparative, interventional case series.

Participants: One hundred thirty-five patients undergoing 141 MSE procedures.

Methods: A prospective series of 141 MSE procedures for LM and LMM over a 10-year period (1993–2002) in a single-center Mohs surgical unit.

Main Outcome Measures: Recurrence, site, size of LM or LMM, invasiveness, prior recurrence, clear margin of excision, size of final defect, and number of levels required for complete excision.

Results: One hundred forty-one MSE procedures, of which 23% (32/141) were for LMM and 19% (27/141) were for periocular lesions. Location or prior recurrence were not predictive of invasive disease; however, the size distribution of the initial lesion ($P = 0.0354$) and the final defect after MSE ($P = 0.0183$) were larger in LMM. Thirty-one percent of LM and 14% of LMM less than 1 mm thick required larger than 5-mm and 1-cm margins, respectively, for complete excision. Mean follow-up of 32 months (range, 1–100 months) revealed 4 recurrences (3%), of which two were periocular ($P = 0.188$).

Conclusions: Our review is the largest prospective series of MSE for LM and LMM and suggests that it is the treatment of choice in these forms of melanoma. Mapped serial excision offers a high early cure rate in conjunction with tissue conservation, which is of particular relevance in the periocular region. There were no significant differences between periocular LM and LMM and those found elsewhere in the head and neck region. It also appears that the current recommendations of 5-mm margins for in situ melanoma (LM) and 1-cm margins for melanoma less than 1 mm thick are insufficient for complete excision of LM or LMM, emphasizing the importance of margin-controlled excision of these lesions. *Ophthalmology 2003;110:2011–2018 © 2003 by the American Academy of Ophthalmology.*

Cutaneous malignant melanoma accounts for only 1% of malignant eyelid tumors; however, it is the leading cause of death from primary skin tumors.[1] The common forms of melanoma in the periocular region are lentigo maligna (LM), lentigo maligna melanoma (LMM), and nodular melanoma.

Originally received: October 20, 2002.
Accepted: March 17, 2003. Manuscript no. 220667.

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Presented at the annual meeting of the American Academy of Ophthalmologists, Orlando, Florida, October 2002.

The authors have no commercial interests in the products or devices mentioned herein.

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Lentigo maligna describes a very slowly progressive, irregularly pigmented macule found most commonly on the face of elderly, sun-damaged individuals. In Australia, the annual incidence of LM has been estimated at 1.3 in 100,000, with the most significant risk factor being ultraviolet radiation exposure.[2] Although there is some controversy over whether LM represents melanocytic dysplasia or melanoma in situ,[3–5] it is the authors' belief that this preinvasive condition should be regarded as melanoma in situ. However, the risk of progression to invasive LMM is not known because no longitudinal prospective studies are available. Although figures as high as 30% to 50% have been quoted in the literature, the true value is likely to be considerably lower.[3] Using incidence and prevalence data, Weinstock and Sober[6] estimated the lifetime risk of developing LMM to be 4.7% for a 45-year-old with LM. As soon as invasive disease has occurred, however, the prognosis for LMM, including local recurrence and survival, is no different from other forms of invasive melanoma if tumor thickness and other prognostic variables are taken into ac-

ISSN 0161-6420/03/$–see front matter
doi:10.1016/S0161-6420(03)00670-5

count.[3,7] A variety of methods have been used in the management of LM, including surgical excision as well as destructive methods such as cryotherapy, radiotherapy, topical treatment with azelaic acid, and curettage electrodesiccation.[8] The destructive techniques, however, may spare deep periadnexal melanocytes and are associated with high rates of tumor recurrence.[3]

Surgical excision has the advantages of treating these deep periadnexal melanocytes, detecting unsuspected invasive melanoma, and permitting histologic assessment of the margins for atypical melanocytes beyond the clinically apparent borders.[9] In the case of unsuspected invasive disease, it also provides prognostic information by enabling measurement of tumor thickness. However, even surgical excision of LM or LMM has only a 90% cure rate.[10,11] The fact that the atypical melanocytes in LM often extend beyond the clinically apparent margins is thought to explain this relatively high recurrence rate.[3,12]

Mohs micrographic surgery (MMS) is a method of tumor excision with frozen-section margin assessment. It is a tissue-conserving technique with a higher cure rate than conventional surgery.[1] There are difficulties, however, using standard frozen sections in the interpretation of melanocytes and melanoma cells, and the identification of single-cell melanocytic proliferations, typically seen in the periphery of LM.[3]

Rush processing of paraffin-embedded sections in combination with MMS has emerged in recent years as a treatment option for both LM and LMM. These mapped serial excision (MSE) techniques combine the margin control and tissue conservation achieved with MMS, with the high-quality histopathologic tissue morphologic features of paraffin sections. In the past decade, MSE for LM and LMM, has been reported to have a recurrence rate of approximately 3%, at mean follow-up of 2 to 3 years, using a variety of paraffin-embedded tissue-sectioning techniques.[12–18]

The aim of this study was to report the early cure rate for LM and LMM using MSE, with vertically cut paraffin-embedded sections, in a single-center Mohs unit over a 10-year period. A secondary aim was to identify any features peculiar to periocular LM and LMM that may predispose to a higher risk of recurrence in comparison with lesions elsewhere on the head and neck. It is known that cutaneous tumors, such as basal cell carcinoma, are associated with a higher recurrence rate in the periocular region[19]; however, to date the recurrence of periocular LM and LMM after MSE has not been studied.

Materials and Methods

A single-center, prospective, noncomparative, interventional case series of 135 consecutive patients with head and neck, including periocular LM or LMM, undergoing MMS with tissue mapping and vertical paraffin sections (MSE), was carried out between March 1993 and February 2002.

Inclusion criteria were histologically confirmed LM or LMM, more than 1 cm in size, occurring on the head and neck. All patients were tertiary referrals and were excluded either by the referring clinician or the treating surgeon if in poor general health or not fit for surgery. All patients gave informed consent before MSE, and all surgical excisions were carried out at the Hill Day Surgery by two surgeons (SCH or DCH). The study was given approval by the local research ethics committee.

Periocular was defined as any lesion predominantly involving either the upper or lower eyelid or the medial or lateral canthus. *Lentigo maligna* was defined as melanoma confined to the epidermis only (Clark level I, melanoma in situ). *Lentigo maligna melanoma* was defined as Clark level II or higher.

The methods used were as described previously by Hill and Gramp.[15] The clinical diagnosis was confirmed histologically to be either LM or LMM by prior shave, punch, or incisional biopsy from the central most pigmented or thickest areas, or both, and a Wood's light was used to help outline the margins of the lesion before surgery. A 5-mm margin from the apparent borders of the tumor was outlined where achievable, before carrying out excision under local anesthetic, to the level of the deep subcutaneous layer. The excised specimen was mapped and dyed and was sent to the pathologist in formalin. A simple dressing was applied to the wound with an antibiotic ointment, and the patient was reviewed the next day after receipt of the results of the pathologic analysis.

The pathologic examination consisted of orientating a formalin-fixed specimen, according to marker dyes and the accompanying color-coded diagram, and preparing vertically cut sections at 1-mm intervals with block identification. After routine paraffin embedding and staining with hematoxylin–eosin, the sections were examined. The sections were examined by two experienced dermatopathologists who used minimum criteria of confluent single-cell proliferation along the dermoepidermal junction and the presence of confluent cytologic atypia to distinguish melanocytic hyperplasia from melanoma in situ. Areas of single cell or random atypia were not considered part of the lesion.

The results were conveyed by telephone within 24 hours, and the site(s) of any incomplete excision were faxed to the dermatologist.

If the pathologist reported incomplete excision, then a further 5-mm excision, where possible, at the site of any positive margin (as indicated by the pathologist) was carried out and sent for histopathologic analysis. Each session of surgical excision was defined as a "level of excision."

The minimum and maximum diameter of the clinically apparent lesion and the final surgical defect was measured using a straight rule. The defect was repaired, either by the dermatologist or an oculoplastic or plastic surgeon after histologic confirmation of clear margins. The margin of complete excision was defined by the number of 5-mm levels required.

Details recorded on a data spreadsheet included patient details, site and histologic features of the lesion (including Clark's level and Breslow thickness), minimum and maximum diameters of the clinically apparent lesion and final defect, details of previous tumor occurrence and treatment, and number of 5-mm levels required to achieve complete excision. All patients were contacted by telephone and invited to return for clinical review during the month of February 2002, and for those unable to attend, a telephone interview aimed at determining recurrence was conducted. The primary outcome measure was recurrence of LM or LMM. Secondary outcome measures were clinical features associated with periocular site, including size, invasiveness, previous recurrence of LM or LMM, size of defect, and number of 5-mm levels required for complete excision.

Statistical Analysis

Associations between categorical variables were analyzed using chi-square tests and the Fisher exact test, if expected values were less than 5. Continuous data were analyzed using a *t* test and were described as mean and standard deviation (mean ± SD). The