

# Treatment of Lentigo Maligna

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*Lentigo maligna (LM) is an indolent form of melanoma in situ with the potential to progress to invasive melanoma. Early detection and adequate treatment prior to development to invasive melanoma are essential. Definitive excision with negative margins is currently the treatment of choice for LM. Conventional excision, Mohs micrographic surgical excision, and nonexcisional methods of treatment of LM will be discussed.*

**L**entigo maligna (LM) occurs predominantly on sun exposed areas of the head and neck in older adults (Figure).<sup>1</sup> There has been controversy as to whether LM represents a precancerous lesion rather than a skin cancer; however, the threat of progression to invasive lentigo maligna melanoma (LMM) exists.<sup>2</sup> Because studies have shown that prognosis of LMM is dependent on the depth of invasion, as with other subtypes of invasive melanoma, detection and treatment of LM prior to progression to invasive disease is necessary.<sup>3</sup> Surgical excision with negative margins is the treatment of choice for LM.<sup>1</sup> Both conventional surgical excision and Mohs micrographic surgery (MMS) have been used successfully in the treatment of LM<sup>4</sup>; however, nonexcisional methods of tumor eradication, including cryosurgery,<sup>5</sup> laser ablation,<sup>6-8</sup> radiation,<sup>9,10</sup> and intralesional<sup>11</sup> and topical therapies,<sup>12,13</sup> also have been used with variable degrees of success.

## Surgical Excision

Surgical excision with negative margins is the mainstay of therapy of LM. Margins of 0.5 to 1.0 cm of clinically uninvolved tissue are currently suggested for the treatment of melanoma in situ.<sup>14</sup> Use of a Wood's lamp may be helpful in determination of subclinical extension. Obtaining a tumor-free plane may be more difficult in LM because of the presence of perilesional melanocytic hyperplasia. In addition, subclinical extension may increase with lesional diameter. In one study, it was found that subclinical tumors extended as far as 1.0 cm beyond clinical margins in lesions larger



Lentigo maligna most commonly appears as a hyperpigmented macule or patch on the head and neck. (Photograph courtesy of Yale Dermatology Residents' Slide Collection.)

than 3 cm in diameter.<sup>15</sup> The necessity of large margins may lead to compromised function or cosmesis, especially when treating lesions on the face.

## Staged Excision

Staged excision allows for confirmation of negative margins with delayed repair and preservation of function and cosmesis. Clayton et al<sup>16</sup> reported treatment of 77 patients with LM with margin control by rush permanent sections. Recurrent LM was noted in one patient. In a study by Johnson et al,<sup>17</sup> successful treatment of 35 patients with LM and LMM was achieved by the "square" procedure. After determination of subclinical extension by examination under Wood's lamp, a surgical margin is outlined with angled corners to facilitate processing. A peripheral strip of 2- to 4-mm tissue is excised and mapped prior to permanent section processing. Positive margins and the remaining island of tumor are extirpated in directed fashion in subsequent procedures. Repair was performed after tumor-free margins were achieved. The authors report no recurrences in 35 patients in a follow-up period of 2 years.<sup>17</sup>

Although staged excision offers the advantage of confirmation of tumor-free margins prior to repair,

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## Treatment Modalities for Lentigo Maligna

- Surgical excision
- Staged excision
- Mohs micrographic surgery
- Modified Mohs micrographic surgery
- Laser surgery
- Radiation therapy
- Cryosurgery
- Intralesional interferon

the completed procedure is performed over several visits. Some patients may find this inconvenient, and many would prefer to have their procedures completed in one day. MMS has been used in an attempt to optimize margin control and efficiency in treatment of LM.

### Mohs Micrographic Surgery

MMS is performed by specially trained dermatologic surgeons in an outpatient setting.<sup>18</sup> The tumor is tangentially excised, frozen sections are examined by the Mohs surgeon, and residual tumor is removed in a directed fashion in subsequent stages. MMS offers the advantage of examination of virtually 100% of the peripheral margin rather than 1% to 3% examined by conventional sections. MMS offers optimal patient convenience because tumors can be excised and repairs performed in a single day.

Of course, extirpation by MMS depends on the ability to detect melanoma cells on frozen section. Some controversy exists as to whether melanoma cells can be detected with adequate sensitivity on frozen sections. Niell et al<sup>19</sup> reported significant differences in tumor thickness values for melanoma obtained by frozen and paraffin sections. Zitelli et al<sup>20</sup> reported detection of melanoma cells on frozen section with 100% sensitivity and 90% specificity. Furthermore, in another study, Zitelli et al<sup>21</sup> reported an overall cure rate of greater than 99% at 5 years for melanoma treated by MMS. In an attempt to optimize detection of malignant melanocytes, some surgeons have modified the Mohs technique by using special histologic stains.

### Modified Mohs Micrographic Surgery

Special histologic stains have been used in an effort to increase sensitivity and specificity of detection of malignant melanocytes at the margins of LM. Gross et al<sup>22</sup> reported successful treatment of 2 patients with

LM using a rapid Mel-5 staining technique. Both patients remained tumor free at 15 and 18 months. Zalla et al<sup>23</sup> reported successful treatment of LM using melan-A, HMB-45, Mel-5, and S-100.

Permanent sections have been used in an attempt to aid recognition of malignant melanocytes in MMS for LM. Cohen et al<sup>24,25</sup> report successful treatment in 45 patients with LM and LMM over a mean follow-up period of 29.2 months. In a follow-up study, they reported one recurrence in 45 patients over a follow-up period of 50 months for an overall cure rate of 98%. As with other types of staged procedures, extirpation and repair takes place over several days.

Although surgery remains the treatment of choice for LM, some patients are not ideal candidates to undergo invasive procedures. In cases where surgery may be contraindicated, the treating physician may choose to pursue alternatives to invasive procedures.

### Laser Surgery

Laser surgery is another treatment option for LM. Treatment is based on selective destruction of melanocytes according to the theory of selective photothermolysis.<sup>26</sup> Arndt<sup>6</sup> reported treatment of LM on the bridge of the nose using the argon laser. The patient remained free of tumor for 3 years. Successful treatment of LM using the Q-switched ruby laser was reported by Thissen and Westerhof.<sup>8</sup> They reported successful ablation after 3 treatments with no recurrence at 1 year. Kauvar and Geronemus<sup>27</sup> reported successful eradication of LM in 3 of 4 patients with LM treated by Q-switched ruby laser during a follow-up period ranging from 6 to 24 months. Amelanotic LM developed in one patient after one year. Treatment failures also have been reported by Lee et al.<sup>28</sup> It was felt that treatment failures may have been due to inadequate depth of penetration. Orten et al<sup>7</sup> reported treatment of LM using the Q-switched Nd:YAG laser, which can emit light at wavelengths of 532 or 1064 nm. The 532-nm wavelength is better absorbed by melanin, but the 1064-nm wavelength offers the benefit of deeper penetration. Not surprisingly, the most encouraging results were reported for 3 patients who were treated with both wavelengths. Two patients showed complete eradication with no sign of recurrence after 3.5 years. The third patient showed a partial response but died from other causes prior to completion of treatment.<sup>7</sup>

Although these results show some promise, it must be stressed that patients treated by laser for LM must be followed closely for development of recurrent or invasive disease. Eradication of pigment makes clinical evaluation more difficult while predisposing for development of amelanotic melanoma.

### Other Modalities

Radiation therapy has been used recently in the treatment of LM. In a study by Schmid-Wendtner et al,<sup>9</sup> 42 patients with LM were treated with fractionated radiation therapy. The authors reported no recurrences during a follow-up period that ranged up to 96 months. Tsang et al<sup>10</sup> treated 54 patients using orthovoltage radiation. They reported variance of cure rates with lesion size and patient age. In general, they reported a 96% cure rate after 3 years in younger patients with smaller lesions and a control rate of 86% after 5 years in older patients with larger lesions. They reported poor cosmesis, characterized by pallor, atrophy and telangiectasias, in 11% of patients.<sup>10</sup>

Cryosurgery has been used in the treatment of LM. In one study by Kuflik and Gage,<sup>5</sup> 30 patients with lesions ranging in size from 1.3 to 4.5 cm were treated with cryosurgery using the open spray technique. The authors reported a 6.6% rate of recurrence and that recurrences were successfully retreated. Potential disadvantages of cryosurgery include the lack of margin control and the risk for hypopigmentation and hypertrophic scarring.

Interferon alfa is a biological response modifier that is currently used in the treatment of stage III melanoma.<sup>29</sup> For this indication, interferon alfa is administered subcutaneously. Side effects such as fever, chills, and flulike symptoms are common. Interferon alfa acts via immunomodulation and antiproliferative effects on melanocytes.<sup>30</sup> Treatment of LM using intralesional interferon alfa was recently reported by Cornejo et al.<sup>31</sup> They reported successful treatment of 11 lesions in 10 patients using 3 to 6 million units administered intralesionally 3 times weekly for a total of 12 to 29 doses. Intralesional interferon alfa also was used successfully in the treatment of recurrent LM of the eyelid in a patient with primary acquired melanosis.<sup>11</sup> Side effects, including fever, chills and flulike symptoms, were reported during the first 24 hours following injections.

Topical agents including azelaic acid,<sup>13</sup> 5-fluorouracil,<sup>12</sup> and imiquimod<sup>32</sup> also have been used in the treatment of LM. Recently, Ahmed and Berth-Jones<sup>32</sup> reported clinical and histologic cure of LM after a 7-month course of treatment with imiquimod. As with other nonexcisional treatment modalities, these methods lack the benefit of margin control.

### Conclusion

LM is a form of melanoma in situ with the potential for progression to invasive melanoma. Surgical excision with clear margins remains the treatment of

choice, however, ablative therapies can be attempted in selected patients in whom surgery is contraindicated. Regardless of treatment method, patients must be monitored regularly for development of recurrent or invasive disease.

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