Diagnosis of Lentigo Maligna Melanoma

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Conflict of Interest: None
Topics

• Epidemiology and Natural History
• Clinical and Histologic Presentations
• Diagnostic Challenges and Modalities
• Treatment Options
Epidemiology

- Sun exposed sites
- Elderly patients
- Incidence
  - 1.3/100,000 in Australia\(^1\)
  - 0.8/100,000 in US\(^2\)
- Most common subtype of melanoma on face
- Long term cumulative UVR

1. Holman CD, Int J Cancer 1980
2. Newell GR, Cancer Res. 1988
Natural History

- The majority of lesions are slowly growing intraepidermal melanocytic proliferations.
- When invasion is detected, it is usually minimal (Clark level II).
- A small subset of LMs progresses rapidly to invasive melanoma.
- A small subset is associated with desmoplastic melanoma.
Diagnostic Challenges

Differential Diagnoses include:

• Pigmented actinic keratosis
• Solar lentigo
• Seborrheic keratosis
• Pigmented BCCs
• LPLKs
Diagnostic Modalities

• Careful clinical exam, include palpation
• Woods light
• Multiple mapping biopsies
• Control biopsy of sun damaged skin
• Dermoscopy
• Confocal reflectance microscopy
Diagnostic Modalities

- Careful clinical exam, include palpation
- Woods light
- Multiple mapping biopsies
- Control biopsy of sun damaged skin
- Dermoscopy
- Confocal reflectance microscopy
Dermoscopy

- Powerful tool to aid the diagnosis of benign vs. malignant pigmented skin lesions.
- A hand-held microscope that provides detailed visualization of the structures contained within the epidermis, epidermal-dermal junction, and papillary dermis not visible to the naked eye.
Clinical Exam

Light
Addition of alcohol oil
Application of dermoscopy
Networks
Globules

Networks
Lentigo Maligna Melanoma

- Asymmetric pigmented follicular openings
- Formation of rhomboidal structures
- Slat-gray dots and globules
- Obliteration of hair follicles
- Change over time
- Polymorphous vessels
Progression Model For Lentigo Maligna

- Dots aggregated around hair follicle
- Rhomboidal structures
- Homogenous areas
- Homogenous areas
- Short streaks
- Melanoma cells within the follicle proliferate and invade adjacent dermis
- Hair follicle were respected
- Obliterated hair follicles
Asymmetric pigmented follicular openings
Asymmetric pigmented follicular openings
Asymmetric pigmented follicular openings
Slate gray dots and globules progressing to short streaks
Slate gray dots and globules progressing to short streaks
Slate gray dots and globules progressing to short streaks
Slate gray dots and globules progressing to short streaks
Streaks progressing to dark rhomboidal structures
Streaks progressing to dark rhomboidal structures
Streaks progressing to dark rhomboidal structures
Homogeneous areas with hair follicles respected
Homogeneous areas with obliterated hair follicles
Polymorphous vessels

Focal dark structureless areas
Differentiating
LM vs. AK vs. LPLK

Clue: Quality and distribution of the “granular particles”
Lentigo Maligna
Pigmented Actinic Keratosis
Lichen planus-like keratosis
Pigmented Actinic Keratosis

- Very broad pseudonetwork
Challenging Cases
Superior Cheek: LM
Inferior Cheek: AK
The Role of Confocal Laser Microscope
Subsurface Imaging
Confocal Laser Microscope

Technology:
• live \textit{in vivo} imaging
• high resolution
  • 0.5-1.0 \textmu m (lateral)
  • 3-5 \textmu m (axial)
• visualization of nuclear, cellular architecture
• max depth 350 \textmu m of the skin
• Field of view: 0.4 x 0.4 cm
Confocal Microscope

- light from outside focal plane optically rejected
- only in-focus information collected (resolution 5 µm)
- can be focussed below specimen surface to isolate sub-surface images (max depth 400 µm = papillary dermis)
- Incremental movement of the focal depth produces 3D image sets
Imaging Modes

- Mosaic view
- Stack view
Imaging Mode: Mosaic

Field of view: 0.4 x 0.4 cm
8x8 images stitched together
The light source moves horizontally over a 2D grid.
Imaging Mode: stack

Field of view: 0.5 x 0.5mm
RCM imaging of normal intact skin
Stratum corneum

0.9 NA, 30X

0.5 mm
Stratum granulosum
Stratum spinosum

0.9 NA, 30X

0.5 mm
Stratum basalis

0.5 mm

0.9 NA, 30X
Dermal Papillae

0.9 NA, 30X

0.5 mm
Normal Epidermis
Lentigo Maligna
Normal Epidermis
Thank You
Sqwang01@yahoo.com
612 910 8088
Therapeutic Options

• Surgery is the treatment of choice
# Therapeutic Options

## Table 1. Comparative Analysis of Different Surgical Techniques for Treatment of Lentigo Maligna and Lentigo Maligna Melanoma

<table>
<thead>
<tr>
<th></th>
<th>Standard Excision$^{16,18,23}$</th>
<th>MMS$^{24}$</th>
<th>MMS Followed by Rush Permanent Sections$^{26}$</th>
<th>“Slow MMS”$^{27}$</th>
<th>“Square” Procedure$^{21,25}$</th>
<th>Staged, Vertical Edge Excision With Rush Permanent Sections$^{3*}$</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Angle of excision</strong></td>
<td>90°</td>
<td>45° or 90°</td>
<td>45°</td>
<td>45°</td>
<td>90°</td>
<td>90°</td>
</tr>
<tr>
<td><strong>Margin size†</strong></td>
<td>2-10 mm</td>
<td>2-3 mm (plus 3-mm initial margin excised with central tumor)</td>
<td>4-6 mm‡</td>
<td>2-5 mm</td>
<td>5-10 mm</td>
<td>2-3 mm</td>
</tr>
<tr>
<td><strong>Tissue-mapping technique</strong></td>
<td>Varies; none to orientation to face of clock</td>
<td>Standard MMS mapping</td>
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<td>Tissue “strips” oriented and mapped to face of clock</td>
<td>Permanent</td>
</tr>
<tr>
<td><strong>Tissue fixation method</strong></td>
<td>Permanent</td>
<td>Frozen</td>
<td>Permanent and frozen</td>
<td>Permanent</td>
<td>Permanent</td>
<td>Permanent</td>
</tr>
<tr>
<td><strong>Reader of margin histologic findings</strong></td>
<td>Pathologist</td>
<td>MMS surgeon</td>
<td>MMS surgeon and pathologist</td>
<td>Pathologist</td>
<td>Pathologist</td>
<td>Pathologist</td>
</tr>
<tr>
<td><strong>Sectioning orientation</strong></td>
<td>Bread loaf</td>
<td>En face (horizontal or vertical)</td>
<td>En face (horizontal)</td>
<td>En face (horizontal)</td>
<td>En face (vertical)</td>
<td>Radial</td>
</tr>
<tr>
<td><strong>Duration of follow-up§</strong></td>
<td>3-3½ y$^{18,20}$, 42 mo$^{24}$</td>
<td>5 y</td>
<td>58 mo</td>
<td>22 mo</td>
<td>Not reported</td>
<td>57 mo</td>
</tr>
<tr>
<td><strong>Recurrence rate§</strong></td>
<td>6/68 (8.8%)$^{18,20}$, 16/81 (20%)$^{24}$</td>
<td>1/184 (0.5%)</td>
<td></td>
<td>1/38 (2.6%)</td>
<td>3/106 (2.8%)</td>
<td>0/35</td>
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## Therapeutic Options

### Standard Excision
- 5mm margin for LM
- 1992 NIH consensus panel
- Inadequate surgical margin
- High local recurrence rate of 15-20%

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### Therapeutic Options

**Mohs Surgery**
- Experience dependent.
- Require immunostains (e.g., MART-1).
- Enface section
- Difficult to differentiate true LM vs. “background” sun-induced melanocyte atypia.

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Bub et al Arch Derm 2004
LM: Frozen vs Permanent Sections

Frozen section

Paraffin-embedded section
Therapeutic Options

Staged Excision
- Inconvenience
- close collaboration with the pathologist

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</tr>
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<td>4-6 mm‡</td>
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<td>3/106 (2.8%)</td>
<td>0/35</td>
<td>3/62 (4.8%)</td>
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MSKCC SERIAL EXCISION TECHNIQUE

- Woods light marking
- Initial 5, 7, 10 mm margin
- Central pigmented lesion excised
- Margins excised
- 12-3, 3-6, 6-9, 9-12
- Await pathology 24 hours
- Re-excise as needed
Tumor Center and Distinct Margin Areas Are Submitted Separately
Distance between Tumor and Margin
Staged excision versus Mohs micrographic surgery for lentigo maligna and lentigo maligna melanoma.

Walling HW, Scupham RK, Bean AK, Ceilley RI.

hobartwalling@yahoo.com

BACKGROUND: Lentigo maligna (LM) is a relatively common tumor with increasing prevalence and substantial morbidity. A variety of treatment modalities are available, though margin-control surgery offers the highest cure rate. We were interested in comparing long-term outcomes of Mohs micrographic surgery (MMS) versus staged excision with permanent sections (SE) for treating LM or LM melanoma (LMM). METHODS: Comparative study consisting of retrospective chart review from our private practice. RESULTS: Fifty-seven patients (31 male, 26 female, mean age at diagnosis 69.1 +/- 10.1 years) were treated in our office for LM (50) or LMM (9) between January 1986 and December 2001. Forty-one tumors (71%) were located on the head and neck. Fifty-three of the 59 tumors (90%) were primary, and 6/59 (10%) were recurrent at the time of initial treatment. Forty-one tumors (36 LM, 5 LMM) were treated with SE, and 18 (14 LM, 4 LMM) were treated with MMS. The mean preoperative lesion size (1.5 +/- 0.2 cm² for SE; 1.2 +/- 0.4 cm² for MMS), mean postoperative defect size (7.1 +/- 1 cm² for SE; 7.1 +/- 1.4 cm² for MMS), and the ratio of postoperative defect to preoperative lesion size (7.9-fold increase for SE, 11.2-fold increase for MMS) were similar between the cohorts. Mean number of stages for clear margins were similar, with 1.8 +/- 0.2 stages (range: 1-7) for SE and 2.0 +/- 0.2 stages (range: 1-4) for MMS; clear margins were obtained in one or two stages in 85% of cases for SE and in 67% for MMS. Three recurrences (3/41; 7.3%) occurred in the SE group while 6 recurrences (6/18; 33%) occurred in the MMS group (P < .025). The mean follow-up duration was 95 months (range: 60-240) in the SE group and 117.5 months (range: 61-157) in the MMS group. LIMITATIONS: Results are limited to a single practice site and fewer patients underwent MMS compared to SE. Patients were not randomized as cases were ascertained retrospectively. CONCLUSION: Staged excision of LM and LMM is associated with a significantly lower recurrence rate with no difference in surgical defect size compared to MMS. To our knowledge, this is the first study directly comparing these two surgical techniques for managing this form of melanoma. Our extended follow-up duration exceeds that of most previous reports.

Publication Types:
- Comparative Study

PMID: 17870430 [PubMed - indexed for MEDLINE]
Therapeutic Options

• Surgery is the treatment of choice

• Superficial treatments
  – LN2
    • 10-50% recurrence rate$^{1-2}$
  – Radiotherapy
    • Farshad et al 2002: retrospective review of 150 patients, 2yr follow up, a 7% recurrence rate
  – Aldara
  – Laser, 5FU, ED&C
Candidates For Alternative Treatment

- Patient refuses surgery
- Poor surgical candidate
- Poor health and multiple medical problem
- Advanced age
- Lesion too large
- difficult anatomic location
Imiquimod: a novel treatment for lentigo maligna

I.AHMED AND J.BERTH-JONES

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Accepted for publication 8 May 2000

Summary

Lentigo maligna is the in situ phase of lentigo maligna melanoma, and if left untreated it may progress to invasive melanoma. It most commonly occurs on the exposed sites of the face and neck of middle-aged or elderly patients. Conventional surgery using a 5–10 mm margin is the recommended treatment; however, lesions can be quite large and surgical removal may involve extensive plastic repair. We report an elderly patient with a large lentigo maligna on the scalp who was reluctant to have surgery. We tried topical imiquimod 5% cream (Aldara®), a local immunomodulator, which has recently become available for the treatment of external genital and perianal warts. Initially used over a test area and then over the whole of the lesion, for a total of 7 months, the imiquimod cream resulted in complete clinical and histological cure. The patient has been followed up for 9 months without evidence of recurrence.

Key words: imiquimod cream, immune modulation, lentigo maligna, treatment
### Table. Patient Characteristics

<table>
<thead>
<tr>
<th>Patient No./Sex/Age, y</th>
<th>Lesion Location</th>
<th>Lesion Size, cm</th>
<th>Duration, wk&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Application Frequency, No.</th>
<th>Inflammatory Response</th>
<th>Outcome</th>
<th>Follow-up, mo</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/F/85</td>
<td>Left cheek</td>
<td>2.8 x 1.5</td>
<td>4 (2)</td>
<td>3/wk</td>
<td>Strong</td>
<td>PCC; HC; persisting turgid redness</td>
<td>22</td>
</tr>
<tr>
<td>2/F/66</td>
<td>Right cheek</td>
<td>1.3 x 1.5</td>
<td>13 (8)</td>
<td>5/wk</td>
<td>Strong</td>
<td>CCC; persisting telangiectasia</td>
<td>21</td>
</tr>
<tr>
<td>3/F/72</td>
<td>Left cheek</td>
<td>1.0 x 1.0</td>
<td>8 (4)</td>
<td>2/d</td>
<td>Severe</td>
<td>PCC; HC; persisting telangiectasia</td>
<td>31</td>
</tr>
<tr>
<td>4/F/95</td>
<td>Left cheek</td>
<td>0.5 x 1.8</td>
<td>3 (2)</td>
<td>1/d</td>
<td>Strong</td>
<td>CCC</td>
<td>16</td>
</tr>
<tr>
<td>5/F/84</td>
<td>Left neck</td>
<td>1.5 x 2.0</td>
<td>5 (3)</td>
<td>2/d</td>
<td>Moderate</td>
<td>CCC</td>
<td>17</td>
</tr>
<tr>
<td>6/F/68</td>
<td>Right cheek</td>
<td>3.5 x 2.5</td>
<td>10 (3)</td>
<td>1/d; after 3 wk, 2/d for 2 wk plus occlusion</td>
<td>Strong</td>
<td>CCC</td>
<td>19</td>
</tr>
<tr>
<td>7/F/81</td>
<td>Right cheek</td>
<td>2.0 x 1.5</td>
<td>13 (6)</td>
<td>1/d; after 4 wk, 2/d</td>
<td>Mild</td>
<td>CCC; persisting telangiectasia</td>
<td>16</td>
</tr>
<tr>
<td>8/F/78</td>
<td>Left lower eyelid</td>
<td>0.5 x 0.5</td>
<td>8 (4)</td>
<td>5/wk plus occlusion</td>
<td>Strong</td>
<td>CCC</td>
<td>19</td>
</tr>
<tr>
<td>9/F/78</td>
<td>Left cheek</td>
<td>4.2 x 6.2</td>
<td>7 (6)</td>
<td>2/d</td>
<td>Mild</td>
<td>CCC</td>
<td>22</td>
</tr>
<tr>
<td>10/F/79</td>
<td>Left temple, left lower eyelid, and right alar wing of nose</td>
<td>1.5 x 1.0</td>
<td>6 (3)</td>
<td>1/d; after 3 wk, unique 2 x 2 cryotherapy&lt;sup&gt;b&lt;/sup&gt;</td>
<td>Severe</td>
<td>CCC</td>
<td>18</td>
</tr>
<tr>
<td>11/F/60</td>
<td>Left cheek</td>
<td>3.2 x 1.5</td>
<td>2 (1.5)</td>
<td>2/d</td>
<td>Strong</td>
<td>CCC</td>
<td>18</td>
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<tr>
<td>12/F/71</td>
<td>Left temple</td>
<td>1.5 x 1.5</td>
<td>7 (5)</td>
<td>2/d</td>
<td>Strong</td>
<td>PCC; HC</td>
<td>14</td>
</tr>
<tr>
<td>13/F/61</td>
<td>Left zygomatic arch</td>
<td>2.5 x 1.5</td>
<td>7 (4)</td>
<td>2/d; plus occlusion</td>
<td>Strong</td>
<td>PC; HC</td>
<td>20</td>
</tr>
<tr>
<td>14/F/72</td>
<td>Right temple</td>
<td>2.0 x 1.5</td>
<td>12 (10)</td>
<td>1/d</td>
<td>Severe</td>
<td>CCC</td>
<td>24</td>
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<tr>
<td>15/F/64</td>
<td>Left alar wing of nose</td>
<td>1.5 x 1.0</td>
<td>20 (16)</td>
<td>1/d; after 8 wk, unique 2 x 2 cryotherapy&lt;sup&gt;b&lt;/sup&gt; plus occlusion</td>
<td>Strong</td>
<td>CCC</td>
<td>16</td>
</tr>
<tr>
<td>16/F/76</td>
<td>Left cheek</td>
<td>3.0 x 1.0</td>
<td>2 (1)</td>
<td>2/d</td>
<td>Strong</td>
<td>CCC</td>
<td>16</td>
</tr>
<tr>
<td>17/F/83</td>
<td>Tip of nose</td>
<td>0.5 x 0.5</td>
<td>6 (4)</td>
<td>2/d</td>
<td>Mild</td>
<td>CCC</td>
<td>19</td>
</tr>
<tr>
<td>18/F/70</td>
<td>Left cheek</td>
<td>3.0 x 1.0</td>
<td>5 (3)</td>
<td>2/d</td>
<td>Moderate</td>
<td>CCC</td>
<td>17</td>
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<td>19/F/84</td>
<td>Right cheek</td>
<td>4.0 x 3.0</td>
<td>16 (12)</td>
<td>5/wk; after recurrence, 2/d; after 4 wk, 2/d plus occlusion</td>
<td>Strong</td>
<td>Recurrence at 30 mo</td>
<td>5</td>
</tr>
<tr>
<td>20/M/93</td>
<td>Bridge of nose</td>
<td>1.0 x 0.5</td>
<td>10 (7)</td>
<td>1/d</td>
<td>Strong</td>
<td>PCC; HC</td>
<td>17</td>
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<td>21/M/84</td>
<td>Nose</td>
<td>2.5 x 2.5</td>
<td>8 (6)</td>
<td>2/d</td>
<td>Strong</td>
<td>CCC</td>
<td>18</td>
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<td>22/M/66</td>
<td>Right earlobe</td>
<td>0.7 x 0.5</td>
<td>3 (2)</td>
<td>1/d</td>
<td>Moderate</td>
<td>CCC</td>
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<tr>
<td>23/M/83</td>
<td>Left lower eyelid</td>
<td>0.4 x 0.4</td>
<td>3 (2)</td>
<td>2/d; plus occlusion</td>
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<tr>
<td>24/M/86</td>
<td>Left earlobe</td>
<td>1.0 x 1.0</td>
<td>4 (2)</td>
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<td>25/M/63</td>
<td>Bridge of nose</td>
<td>0.8 x 0.5</td>
<td>4 (1)</td>
<td>2/d</td>
<td>Moderate</td>
<td>CCC</td>
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<td>26/M/79</td>
<td>Right alar wing of nose</td>
<td>0.5 x 0.5</td>
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<td>27/M/50</td>
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<td>7 (5)</td>
<td>1/d</td>
<td>Strong</td>
<td>CCC</td>
<td>18</td>
</tr>
<tr>
<td>28/M/68</td>
<td>Right upper eyelid</td>
<td>0.5 x 0.5</td>
<td>4 (3)</td>
<td>2/d; plus occlusion</td>
<td>Strong</td>
<td>CCC</td>
<td>21</td>
</tr>
<tr>
<td>29/M/72</td>
<td>Right alar wing of nose</td>
<td>0.5 x 1.5</td>
<td>7 (3)</td>
<td>1/d</td>
<td>Strong</td>
<td>CCC</td>
<td>9</td>
</tr>
<tr>
<td>30/M/80</td>
<td>Left cheek</td>
<td>2.5 x 3.5</td>
<td>8 (4)</td>
<td>2/d</td>
<td>Moderate</td>
<td>CCC</td>
<td>10</td>
</tr>
<tr>
<td>31/M/66</td>
<td>Right cheek</td>
<td>2.2 x 4.0</td>
<td>10 (7)</td>
<td>2/d</td>
<td>Strong</td>
<td>CCC</td>
<td>12</td>
</tr>
<tr>
<td>32/M/72</td>
<td>Right cheek</td>
<td>1.5 x 1.0</td>
<td>5 (3)</td>
<td>1/d</td>
<td>Strong</td>
<td>CCC</td>
<td>5</td>
</tr>
</tbody>
</table>

Abbreviations: CCC, complete clinical clearance; HC, histologically confirmed; PCC, partial clinical clearance (residual pigmentation).

<sup>a</sup>Duration of treatment (duration to the point of skin reaction).

<sup>b</sup>Liquid nitrogen cryotherapy using 2 freeze-thaw cycles with a freezing time of 2 seconds each.
Conclusions

• Clinical diagnosis of LMM is difficult.
• Dermoscopy and confocal laser microscopy are valuable diagnostic tools.
• Surgery is the treatment of choice
• Alternative treatments include Aldara and radiation.
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Career Development Award
Future Direction

What if there is a way to map out the surgical border before Mohs surgery?