CUTANEOUS MELANOMA
AN OVERVIEW

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No Disclosures
• 2020: 8000 new cases
• Lifetime probability: 2.1%
• Mortality rate: 3.1 per 100,000
Scenario 1

55F w suspicious upper back pigmented lesion

Question 1: What’s your next step in management?

A. Excisional biopsy
B. Shave biopsy
C. Punch biopsy
D. Refer to dermatologist
E. Refer to plastic surgeon
F. Refer to general surgeon
Question 2: Do you routinely perform skin biopsy in your office?

A. Yes  
B. No
**ABCDEs: Mole or Melanoma?**

- **A**: Asymmetry - One half of a mole does not match the other.
- **B**: Border - The edges are irregular, ragged, notched, or blurred. Normal moles are round or oval.
- **C**: Color - The color is not evenly colored. It may include shades of brown or black, or patches of pink, red, white, or blue.
- **D**: Diameter - The spot is larger than 6 millimeters across.
- **E**: Evolving - The mole is changing in size, shape, or color.

**Mole Features**

<table>
<thead>
<tr>
<th>Feature</th>
<th>Benign</th>
<th>See Doctor</th>
</tr>
</thead>
<tbody>
<tr>
<td>A - Asymmetry</td>
<td><img src="image1" alt="Benign Mole" /></td>
<td><img src="image2" alt="Mole to See Doctor" /></td>
</tr>
<tr>
<td>B - Border</td>
<td><img src="image3" alt="Benign Mole" /></td>
<td><img src="image4" alt="Mole to See Doctor" /></td>
</tr>
<tr>
<td>C - Color</td>
<td><img src="image5" alt="Benign Mole" /></td>
<td><img src="image6" alt="Mole to See Doctor" /></td>
</tr>
<tr>
<td>D - Diameter</td>
<td><img src="image7" alt="Benign Mole" /></td>
<td><img src="image8" alt="Mole to See Doctor" /></td>
</tr>
<tr>
<td>E - Evolving</td>
<td><img src="image9" alt="Benign Mole" /></td>
<td><img src="image10" alt="Mole to See Doctor" /></td>
</tr>
</tbody>
</table>
**Technique of excisional biopsy**

- **Limbs** — excision axis in long axis of the limb, parallel to lymphatic vessels
- **The narrowest margin** 1–3 mm
- **Lymphatic vessels**
- **Completely resected suspicious lesion** has to be histopathological examined
- **Local anaesthesia**
PRINCIPLES OF BIOPSY OF A SUSPICIOUS PIGMENTED LESION

- Excisional biopsy (elliptical, punch, or saucerization/deep shave) with 1- to 3-mm margins preferred. Avoid wider margins to permit accurate subsequent lymphatic mapping.
- The orientation of an elliptical/fusiform excisional biopsy should be planned with definitive wide local excision in mind (eg, longitudinally [axially] and parallel to the underlying lymphatics on the extremities).
- Full-thickness incisional or punch biopsy\(^a\) of clinically thickest or most atypical portion of lesion is acceptable in certain anatomic areas (eg, palm/sole, digit, face, ear) or for very large lesions. Multiple "scouting" biopsies may help guide management for very large lesions. Superficial shave biopsy\(^a,b\) may compromise pathologic diagnosis and complete assessment of Breslow thickness, but is acceptable when the index of suspicion is low. However, a broad shave biopsy may be optimal for histologic assessment for melanoma in situ, lentigo maligna type.
- Repeat narrow-margin excisional biopsy is recommended if an initial partial biopsy is inadequate for diagnosis or microstaging but should not be performed if the initial specimen meets criteria for SLN staging.
<table>
<thead>
<tr>
<th>T Category</th>
<th>Thickness</th>
<th>Ulceration Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>TX: Primary tumor thickness cannot be assessed (eg, diagnosis by curettage)</td>
<td>Not applicable</td>
<td>Not applicable</td>
</tr>
<tr>
<td>T0: No evidence of primary tumor (eg, unknown primary or completely regressed melanoma)</td>
<td>Not applicable</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Tis (melanoma in situ)</td>
<td>≤1 mm</td>
<td>Unknown or unspecified</td>
</tr>
<tr>
<td></td>
<td>&lt;0.8 mm</td>
<td>Without ulceration</td>
</tr>
<tr>
<td></td>
<td>&lt;0.8 mm</td>
<td>With ulceration</td>
</tr>
<tr>
<td></td>
<td>0.8–1.0 mm</td>
<td>With or without ulceration</td>
</tr>
<tr>
<td>T1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>T1a</td>
<td>&lt;1 mm</td>
<td></td>
</tr>
<tr>
<td>T1b</td>
<td></td>
<td></td>
</tr>
<tr>
<td>T2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>T2a</td>
<td>1 – 2 mm</td>
<td></td>
</tr>
<tr>
<td>T2b</td>
<td></td>
<td></td>
</tr>
<tr>
<td>T3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>T3a</td>
<td>2 – 4 mm</td>
<td></td>
</tr>
<tr>
<td>T3b</td>
<td></td>
<td></td>
</tr>
<tr>
<td>T4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>T4a</td>
<td>&gt;4 mm</td>
<td></td>
</tr>
<tr>
<td>T4b</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tumor Thickness</td>
<td>Recommended Clinical Margins$^b$</td>
<td></td>
</tr>
<tr>
<td>-----------------</td>
<td>----------------------------------</td>
<td></td>
</tr>
<tr>
<td>In situ$^a$</td>
<td>0.5–1.0 cm</td>
<td></td>
</tr>
<tr>
<td>≤1.0 mm</td>
<td>1.0 cm (category 1)</td>
<td></td>
</tr>
<tr>
<td>&gt;1.0–2 mm</td>
<td>1–2 cm (category 1)</td>
<td></td>
</tr>
<tr>
<td>&gt;2.0–4 mm</td>
<td>2.0 cm (category 1)</td>
<td></td>
</tr>
<tr>
<td>&gt;4 mm</td>
<td>2.0 cm (category 1)</td>
<td></td>
</tr>
</tbody>
</table>
Table 3. Studies That Evaluated Surgical Margins of Wide Excision of Melanoma

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>N</th>
<th>Follow-up (years)</th>
<th>Thickness (mm)</th>
<th>Margin (cm)</th>
<th>LR</th>
<th>OS</th>
</tr>
</thead>
<tbody>
<tr>
<td>WHO</td>
<td>1991</td>
<td>612</td>
<td>8</td>
<td>≤2</td>
<td>1 vs. ≥3</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Sweden</td>
<td>2000</td>
<td>989</td>
<td>11</td>
<td>&gt;0.8–2.0</td>
<td>2 vs. 5</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Intergroup</td>
<td>2001</td>
<td>468</td>
<td>10</td>
<td>1–4</td>
<td>2 vs. 4</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>France</td>
<td>2003</td>
<td>326</td>
<td>16</td>
<td>≤2</td>
<td>2 vs. 5</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>UK</td>
<td>2016</td>
<td>900</td>
<td>8.8</td>
<td>&gt;2</td>
<td>1 vs. 3</td>
<td>NS</td>
<td>NSa</td>
</tr>
<tr>
<td>Sweden</td>
<td>2011</td>
<td>936</td>
<td>6.7</td>
<td>&gt;2</td>
<td>2 vs. 4</td>
<td>NS</td>
<td>NS</td>
</tr>
</tbody>
</table>

LR, local recurrence; OS, overall survival; NS, non-significant

a Analysis after a median follow-up of 5.7 years showed no significant difference in overall survival or melanoma-specific survival, but analysis after a median follow-up of 8.8 years showed significantly better melanoma-specific survival for patients with 3-cm vs. 1-cm excision margins (unadjusted HR, 1.24; 95% CI, 1.01–1.53; *P* = .041) but no significant improvement in overall survival (unadjusted HR, 1.14; 95% CI, 0.96–1.36; *P* = .14).
Scenario 1

Punch biopsy showed 1.2mm deep melanoma with ulceration

Question 3: What’s your next step in management?

A. Refer for surgery
B. Ultrasound axilla and neck
C. CT Chest/Abdomen/Pelvis
D. MRI Brain
E. PET Scan
CLINICAL/ PATHOLOGIC STAGE WORKUP

Stage IIIA (sentinel node positive) • Consider imaging¹ for baseline staging
• Imaging¹ to evaluate specific signs or symptoms

Stage IIIB/C/D (sentinel node positive) Imaging¹ for baseline staging and to evaluate specific signs or symptoms

Stage III (clinically positive node[s]) See ME-5
Scenario 1

55F underwent wide local excision + SLNB. Sentinel node showed 1 positive lymph node.

Question 4: What’s the next step in management?

A. Completion axillary dissection
B. Imaging (CT, PET)
C. Radiation
D. Chemotherapy
E. Immunotherapy
Final Analysis of DeCOG-SLT Trial: No Survival Benefit for Complete Lymph Node Dissection in Patients With Melanoma With Positive Sentinel Node

Unrke Leiter, MD; Rudolf Stadler, MD, PhD; Comelia Mauch, MD, PhD; Werner Hohenberger, MD; Norbert H. Brockmeyer, MD; Carola Berking, MD; Cord Sunderkötter, MD; Martin Kaatz, MD; Kerstin Schatton, MD; Percy Lehmann, MD; Thomas Vogl, MD; Jens Ulrich, MD; Rudolf Herbst, MD; Wolfgang Gehring, MD; Jan-Christoph Simon, MD; Ulrike Keim, PhD; Daniell Verver, MD; Peter Martus, PhD; and Claus Garbe, MD; on behalf of the German Dermatologic Cooperative Oncology Group.
MSLT-II

AFTER INITIAL SURGERY

Immediate CLND*

Observation with Nodal Basin Ultrasound**

*CLND (Completion Lymph Node Dissection) of affected nodal basin(s) (up to 2)

**Observation with regional nodal ultrasound every 4 months for 2 years, then every 6 months for 3 years, then annually
Who needs a completion axillary dissection?

**American Society of Clinical Oncology (ASCO) – SSO Consensus Guidelines**

- All patients with clinically positive lymph nodes
- CLND or observation = options for patients with low risk micrometastatic disease
- Higher risk features of SLN- Extracapsular extension, microsatellitosis of primary tumor, \( \geq 3 \) involved nodes, \( \geq 2 \) nodal basins and immunosuppression \( \rightarrow \) CLND
• Ultrasound at least q4 months x 2 years, then q6 months x 3
Scenario 2

55F post-op day 7 axillary dissection

Question 5: What’s your next step in management?

A. Observe
B. Aspirate
C. Incision & Drainage
D. Antibiotics
E. Ultrasound
<table>
<thead>
<tr>
<th>DRUG TYPE</th>
<th>EXAMPLES</th>
</tr>
</thead>
<tbody>
<tr>
<td>CTLA-4 inhibitors</td>
<td>Ipilimumab</td>
</tr>
<tr>
<td>PD-1 inhibitors (targeting the “lock”)</td>
<td>Nivolumab</td>
</tr>
<tr>
<td></td>
<td>Pembrolizumab</td>
</tr>
<tr>
<td>PD-L1 inhibitors (targeting the “key”)</td>
<td>Atezolizumab</td>
</tr>
<tr>
<td></td>
<td>Avelumab</td>
</tr>
<tr>
<td></td>
<td>Durvalumab</td>
</tr>
<tr>
<td>Combination therapy</td>
<td>Ipilimumab + nivolumab</td>
</tr>
</tbody>
</table>
ENDOCRINE ORGANS
- e.g., overactive thyroid (hyperthyroidism) or underactive thyroid (hypothyroidism), or inflammation of pituitary gland (hypophysitis)

LUNGS
- e.g., lung inflammation (pneumonitis)

LIVER
- e.g., liver inflammation (hepatitis)

SKIN
- e.g., rash, itching (pruritus), loss of pigment (vitiligo)

GASTROINTESTINAL TRACT
- e.g., diarrhoea, colitis
Managed in outpatient/community setting

Increasing intensity of treatment required

Needs hospital admission and care

Referral to specialist
Strong immunosuppressive therapy

Oral steroids → Intravenous steroids started

Stop treatment* →

Symptomatic therapy

Increasing grade of side effect

Grade 1 MILD

Grade 2 MODERATE

Grade 3 SEVERE

Grade 4 VERY SEVERE

* For some side effects, treatment can be restarted when they subside
Scenario 3

55F with a history of left foot melanoma now presenting w 2 lesions on the shin

Question 6: What’s your next step in management?

A. Biopsy one of the lesions
B. Examine popliteal fossa + groin
C. PET scan
D. Refer to surgeon
E. Refer to BC Cancer
F. All of the above
• **In-Transit Melanoma** - Metastases within regional dermal and subdermal lymphatics 2cm or more from primary melanoma

• 75% develop nodal or distant metastases
Intralesional injection options:

- T-VEC
- BCG
- IL-2
**Isolated limb perfusion**

- HEART-LUNG MACHINE
- Melphalan
  - 60 minutes
  - 40 degrees Celsius

**Isolated limb infusion**

- Melphalan
  - 20-30 minutes
  - 36-39 degrees Celsius
**NEOADJUVANT PHASE**

- **Arm A:** Neoadjuvant nivolumab up to 4 doses (n=20)
  - Randomization stratified by stage and PD-L1 status
  - Patients with resectable clinical stage III or oligometastatic stage IV melanoma

- **Arm B:** Neoadjuvant ipilimumab + nivolumab up to 3 doses (n=20)
  - Baseline sampling
  - On-treatment sampling

**ADJUVANT PHASE**

- Radiographic assessment (ORR by RECIST 1.1)
- Restaging imaging
- Surgical resection
- Pathologic assessment (pCR rate)
- Adjuvant nivolumab up to 13 doses over 6 months
- Surgical sampling
- Adjuvant phase sampling

**Clinical and radiographic follow-up**

**Secondary survival and safety outcomes** (PFS, DMFS, RFS, OS, toxicity)
Questions?