The Sentinel Node in Head and Neck Melanoma

Cutaneous Melanoma: Epidemiology (USA)
- 6th leading cause of cancer among men and women
- 68,720 new cases of invasive melanoma in 2009
- 8,650 deaths from melanoma in 2009

Cutaneous Melanoma: Epidemiology (USA)
- Incidence is on the rise (600% increase over past 50 years)*
  - Increasing faster than any other cancer
  - Lifetime risk:
    - 1/1500 for individual born in 1935
    - 1/250 for individual born in 1980
    - 1/74 for individual born in 2000

Head and Neck Cutaneous Melanoma: Epidemiology (USA)
- 25-30% of melanomas
- Second most common site overall
- More biologically aggressive
- Common anatomic locations
  - Face (40-60%)
  - Scalp (14-49%)
  - Neck (20-29%)
  - Ear (8-11%)

*SEER Data

Risk Factors

- Sun exposure: frequency, age of exposure
- History of blistering sunburns
- Number of nevi
  - > 20 increases relative risk by 3
  - > 100 increases relative risk by 7
  - 50% of melanomas arise in pre-existing nevi
- Other risk factors: fair skin, red hair, freckling
- Family history

Prevention

- Melanocytic nevi develop mainly during childhood/adolescence
  - Preventive measures critical during early life
- Public Education
  - Sun avoidance, protective clothing
  - Sun screen? Not shown to be preventive
- Screening of high-risk populations

Work-up

- American Cancer Society’s ABCD’s
  - A-Asymmetry
  - B-Border irregularity
  - C-Color variation
  - D-Diameter > 6mm
  - (E-Evolution of change)
- History
  - Signs: recent change in size, color, shape
  - Symptoms: Pruritis, crusting, bleeding, tenderness
- Biopsy suspicious lesions
  - Excisional biopsy with 1-2 mm margins
  - Full-thickness incisional or punch biopsy of thickest portion for larger lesions
  - NEVER shave biopsy
Staging (AJCC 2002)

<table>
<thead>
<tr>
<th>T classification</th>
<th>Thickness</th>
<th>Ulceration Status a)</th>
<th>Ulceration Status b)</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1</td>
<td>≤ 1.0 mm</td>
<td>without ulceration</td>
<td>BI/MU</td>
</tr>
<tr>
<td>T2</td>
<td>1.0-2.0 mm</td>
<td>without ulceration</td>
<td>with ulceration</td>
</tr>
<tr>
<td>T3</td>
<td>2.0-4.0 mm</td>
<td>without ulceration</td>
<td>with ulceration</td>
</tr>
<tr>
<td>T4</td>
<td>&gt; 4.0 mm</td>
<td>without ulceration</td>
<td>with ulceration</td>
</tr>
</tbody>
</table>

In-transit satellite metastasis

Staging (AJCC 2002)

<table>
<thead>
<tr>
<th>M classification</th>
<th>Site</th>
<th>Serum Lactate Dehydrogenase</th>
</tr>
</thead>
<tbody>
<tr>
<td>M1a</td>
<td>Distant skin, subcutaneous, or nodal mets</td>
<td>Normal</td>
</tr>
<tr>
<td>M1b</td>
<td>Lung metastases</td>
<td>Normal</td>
</tr>
<tr>
<td>M1c</td>
<td>All other visceral metastases</td>
<td>Normal (Any distant metastasis) Elevated</td>
</tr>
</tbody>
</table>

* Micrometastases are diagnosed after sentinel or elective lymphadenectomy.

(Micrometastases are defined as clinically detectable nodal metastases confirmed by therapeutic lymphadenectomy or when nodal metastasis exhibits gross extracapsular extension.


Staging

- Localized (Stage I, II)
  - T<sub>any</sub> N0 M0
  - Prognostic features
    - Tumor thickness
      - Clark's Level of invasion for (T1)
    - Ulceration

- Regional metastasis (Stage III)
  - T<sub>any</sub> N+ M0
  - Prognostic Features
    - Number of metastatic nodes
    - Micro vs. macroscopic disease
    - Intralymphatic metastasis (in-transit satellites)

- Distant metastasis (Stage IV)
  - T<sub>any</sub> N<sub>any</sub> M+
  - Prognostic features
    - Anatomic site: distant nodal basin, lung, other visceral organs
    - LDH
Treatment

• Primary site: margins determined by tumor thickness
  – Melanoma in situ: 5 mm
  – < 1 mm: 1 cm
  – 1 – 2 mm: 1 – 2 cm
  – > 2 mm: 2 cm
  – Margins modified to accommodate anatomic and cosmetic considerations

Clinically node-positive melanoma

• Stage III Disease
  – Therapeutic lymph node dissection
    • Preserve when possible the SCM, IJ, spinal accessory nerve

Clinically node-positive melanoma

• Stage III Disease
  – Consider primary site, location of positive node(s)
    • Levels I-III (lower face, lip), II-V (auricle), V + occipital and post-auricular nodes (scalp)
    • Superficial parotidectomy (temple, forehead, cheek)
Multiple melanotic periparotid nodes

- 26 year old female presented with regional node recurrence 6 months following wide excision of 0.45 mm thick right neck melanoma
- Imaging showed multiple level II-IV nodes, invasive of SCM

Completed modified radical neck dissection

Clinically node-negative melanoma

- Risk of occult nodal disease: tumor thickness
  - < 1.0 mm: 5%
  - 1 – 2 mm: 15-20%
  - 2 – 4 mm: 25%
  - > 4 mm: 35%
- Higher in young patients, high tumor mitotic rate
- Lower in desmoplastic, lentigo maligna melanoma
Clinically node-negative melanoma

- Role of elective neck dissection
  - 2 prospective studies (WHO Melanoma Group and Mayo Clinic) failed to demonstrate survival benefit for ELND
  - ELND not routinely performed today

Sentinel lymph node biopsy

- Minimally invasive procedure to identify patients harboring occult nodal disease
  - Identifies patients who warrant therapeutic neck dissection and adjuvant therapy
  - Spares ~80% of patients without regional disease the morbidity of a neck dissection and/or parotidectomy

Sentinel lymph node biopsy

- Directs to nodes at risk
  - Cutaneous lymphatic drainage less predictable than mucosal
- Allows more thorough pathologic assessment than typically performed for complete neck dissection specimen

Sentinel lymph node biopsy

- Most sensitive and specific modality for regional staging
- Most important prognostic factor for recurrence and survival*
- AJCC incorporated SLNB into current staging system

Sentinel lymph node biopsy

- Indications for SLNB
  - Thickness: > 1 mm
  - Clark’s Level IV or V
  - Ulceration
  - Extensive regression to 1.0 mm
- Relative indications for SLNB
  - Young age
  - High mitotic rate

- Contraindications for SLNB
  - Evidence of regional or distant metastasis
  - Flap reconstruction performed for primary tumor resection/closure
    - Native lymphatic drainage channels disrupted

Technique of SLNB

- Intradermal injection of technetium-99 sulfur colloid at the primary site
- Serial images taken with gamma camera
- Sentinel nodes marked on skin
  - Typically 2 to 4

- Pre-incision intradermal injection of blue dye
  - Methylene blue
Technique of SLNB

• Use gamma probe for SLN identification

Node Seeker

Neo Probe

Technique of SLNB

• Facial nerve monitor useful

Radio-guided surgery, exploring for blue-colored nodes
Technique of SLNB

- Frozen section inadequate
- Permanent histologic evaluation
  - Serial sectioning (5 microns)
  - H&E staining
  - Immunohistochemistry higher sensitivity
    - S-100 (97%), HMB-45 (75%), Melan-A (96%)

Sentinel lymph node biopsy

- Positive SLNB
  - Therapeutic neck dissection +/- parotidectomy
  - Counseling for adjuvant therapy
    - Interferon alpha-2b
    - Radiation therapy
- Negative SLNB
  - Follow clinically

2 year old male: Superficial parotidectomy and selective neck dissection levels II/III performed 2 weeks following sentinel lymph node biopsy (2/4 positive intra-parotid sentinel lymph nodes)
Outcome data for SLNB

- **Efficacy**
  - Successful SLN identification in 96%*
  - Mean # nodes removed=2.8, range 1-7
  - Regional failure in setting of negative SLN-4.5%*
  - No cranial nerve injuries


Outcome data for SLNB

- **Challenges of H&N SLNB**
  - Higher false negative rate in H&N compared to other anatomic nodal basins
    - Complexity of cervical lymphatics
    - Problem of “shine-through”
- **Safety of H&N SLNB**
  - Damage to vital structures, cranial nerves
  - Intraparotid SLNB
  - There is a learning curve for surgeon
    - ~30 cases to be proficient

H&N SLNB

- **SLN Working Group**
  - 614 H&N melanoma pts underwent SLNB
  - 10.1% positive
  - SLN status most important predictor of disease-free survival
    - Other predictors—tumor thickness, ulceration
  - Scalp site independent predictor of +SLN, recurrence, increased mortality


Outcome data for SLNB

- **MSLT-1 trial:** Stage III patients identified through SLNB had improved survival compared to patients who developed palpable metastasis under a watchful waiting policy

Adjuvant therapy

• Indications for radiation therapy
  – Close or positive margins
  – Bulky nodes, multiple nodes, ECS
  – No comprehensive neck dissection performed
  – Typical dose: 30 Gy given in 5 large fractions (6 Gy per treatment) over 2 ½ weeks

Adjuvant therapy

• Indications for interferon
  – Completely treated Stage III disease
  – No medical contraindication for Interferon
  – Typical regimen: 4 weeks of high-dose IV IFN, followed by 11 months of self-administered SC IFN

Take-home points

• Cutaneous melanoma incidence rising faster than any other cancer
• 25 - 30% of melanomas occur in the head and neck

Take-home points

• Surgery is primary treatment modality for melanoma
• SLNB: minimally invasive technique for assessment of regional nodes in cutaneous melanoma
• Head and neck surgeon should play a key role in the management of this disease