LYMPH NODE DISSECTION FOR MELANOMA

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September 5, 2013
CASE PRESENTATION

- 84 year old male
- PMH: Afib, HTN, CAD s/p MI (2002), Left leg lesion growing in size for 8 months with history of intermittent bleeding and itchiness
- Medications: ASA, Plavix, Verapamil, Hyzaar, Lipitor, Zantac
- NKDA
- SH: Denied tobacco, alcohol, illicit drugs
- FH: No family history of skin cancer
CASE PRESENTATION

• 6/4/13 - Initial surgical evaluation
  • 3x3x1cm raised nodule along the anterior left mid-thigh. There was no lymphadenopathy, surrounding lesions or discoloration

• 6/12/13: Wide local excision of left leg lesion
  • Nodular melanoma
  • Thickness of 1.8cm without lymphovascular invasion.
  • Margins > 2cm except 0.9mm at deep margin
CASE PRESENTATION

- 6/25/13: Mapping lymphangiogram showed one sentinel lymph node in the left inguinal region

- 7/9/13: Postoperative visit revealed 1cm nodule in left inguinal region without evidence of in-transit disease or satellite lesions

- 7/25/13: PET/CT revealed 2 foci of increased uptake in the left inguinal region
CASE PRESENTATION

- 8/15/13: Preoperative lymphangiogram showed 3 sentinel lymph nodes in the left inguinal region

- 8/15/13: re-excision of left leg melanoma site, SLNB frozen section and left inguinal-femoral lymph node dissection
  - Positive frozen section for metastatic melanoma
  - 2/6 inguinal-femoral nodes positive for metastatic melanoma
  - Skin of left thigh negative for melanoma
Questions
GOALS OF PRESENTATION

- Introduction
- Epidemiology and etiology
- Risk factors and precursor lesions
- Diagnosis and clinical presentation
- Staging
- Management of local disease
- Prognosis
- Lymph node biopsy and dissections
- Follow-up
INTRODUCTION

- Melanoma is a cancer of melanocytes – cells of neural crest origin.
EPIDEMIOLOGY

- Melanoma accounts for less than 5% of skin cancer cases but causes the majority of skin cancer deaths
- 8790 melanoma-related deaths (2010)
- 70,230 new melanoma diagnoses in the US (2010)
- Predominantly in Caucasians and least common in African Americans
- Median age is 50 years with greatest incidence in older patients but is one of the most common cancers in young adults
- Incidence rises at a rate of 3% per year
HISTORICAL PERSPECTIVE

• 1787 – Hunter published one of the first accounts of melanoma
• 1806 – Laennec discovered metastatic melanoma deposits in the liver and differentiated them from the more common black tuberculous granulomas and routine carbon deposits
• 1905 – Handley suggested removal of 2 inches of subcutaneous tissue down to the level of the muscle fascia together with radical lymph node removal
HISTORICAL PERSPECTIVE

• 1969 – Clark and associates
  • Classification based on extent of tumor invasion relative to the anatomic layers of the skin and showed that level of invasion was related to survival
  • Not reproducible among pathologists

• 1970 – Breslow
  • Classification based on tumor thickness in millimeters
  • Reproducible among pathologists
  • Excellent correlation with 5-year survival
COMPARISON OF CLARK AND BRESLOW CLASSIFICATIONS
RISK FACTORS

- Exact cause of melanoma is still unknown. However...
  - Personal history of melanoma or other skin cancers
  - Family history of melanoma (5-10% of all melanomas)
  - Fair complexion
  - Reaction to sun exposure (freckling, sunburns) or intense intermittent sun exposure
  - Xeroderma pigmentosum (DNA repair)
  - UVA and UVB radiation (Tanning beds)
PRECURSOR LESIONS

- Dysplastic nevi: 6-15mm flat pigmented lesion with indistinct margins and variable color
PRECURSOR LESIONS

- Giant congenital nevi: > 20 cm in diameter carry 10% lifetime risk of melanoma
PRECURSOR LESIONS

- Spitz nevus (juvenile melanoma): rapidly growing pink/brown benign lesion
FAMILIAL MELANOMA

• Dysplastic nevus syndrome; familial atypical multiple mole-melanoma syndrome (FAMMM), B-K mole syndrome

• Characterized by one or more first or second-degree relatives and large numbers of melanocytic nevi (50-100+)

• Often linked to a family history of pancreatic cancer
DIAGNOSIS

• Asymmetry
• Irregular Border
• Color variations
• Diameter greater than 6mm
• Evolution
DIAGNOSIS

- History and physical – Is there a change?
- Biopsy – Have a low threshold
  - Excisional – most appropriate for pigmented lesions
  - Incisional – for larger lesions; usually via multiple punch biopsies including the thickest portion and portion of normal tissue
HISTOLOGY

• Four major types based on growth pattern and location
  • Superficial spreading melanoma
  • Lentigo maligna melanoma
  • Nodular melanoma
  • Acral lentiginous melanoma
SUPERFICIAL SPREADING MELANOMA

- 70% of melanomas
- Arise from preexisting dysplastic nevi
- Usually flat and average 2cm in diameter but may become irregular and elevated in later stages
NODULAR MELANOMA

- 15% of melanomas
- Early vertical growth into the dermis with minimal radial component
- Typically blue-black ulcerated and may bleed
LENTIGO MALIGNA MELANOMA

- 10% of melanomas
- Lesions appear larger than 3cm and are flat, tan, freckle-like with marked notching of borders
- Occur in sun-exposed areas most commonly in elderly patients

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ACRAL LENTIGINOUS MELANOMA

- 5% of all melanomas
- 35-60% in dark-skinned people
- Confined to the subungual areas and the glabrous skin of the palms and soles
PROGNOSIS

- Histology itself does not predict survival; however, certain histology lend toward later diagnosis or early lymphatic spread
  - Nodular melanomas have an early vertical growth phase
  - Acral lentiginous melanomas may have a delay in diagnosis
  - Superficial spreading often develop from precursor lesions

- Number one predictor of survival is lymph node status followed by tumor depth, ulceration, lymphovascular invasion and mitotic rate
**TABLE 1: TNM staging for cutaneous melanoma**

<table>
<thead>
<tr>
<th>Classification</th>
<th>Thickness (mm)</th>
<th>Ulceration status/mitoses</th>
</tr>
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<tbody>
<tr>
<td>Tis</td>
<td>NA</td>
<td>NA</td>
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<tr>
<td>T1</td>
<td>≤ 1.00</td>
<td>a: Without ulceration and mitosis &lt; 1/mm²</td>
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<td></td>
<td></td>
<td>b: With ulceration and mitosis ≥ 1/mm²</td>
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<tr>
<td>T2</td>
<td>1.01–2.00</td>
<td>a: Without ulceration</td>
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<tr>
<td></td>
<td></td>
<td>b: With ulceration</td>
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<tr>
<td>T3</td>
<td>2.01–4.00</td>
<td>a: Without ulceration</td>
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<tr>
<td></td>
<td></td>
<td>b: With ulceration</td>
</tr>
<tr>
<td>T4</td>
<td>&gt; 4.00</td>
<td>a: Without ulceration</td>
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<tr>
<td></td>
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<td>b: With ulceration</td>
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**Regional nodes (N)**

<table>
<thead>
<tr>
<th>Classification</th>
<th>No. of metastatic nodes</th>
<th>Nodal metastatic burden</th>
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<tbody>
<tr>
<td>N0</td>
<td>0</td>
<td>NA</td>
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<tr>
<td>N1</td>
<td>1</td>
<td>a: Micrometastasis(^a)</td>
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<td>b: Micrometastasis(^b)</td>
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<td>N2</td>
<td>2–3</td>
<td>a: Micrometastasis(^a)</td>
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<td></td>
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<td>b: Micrometastasis(^b)</td>
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<tr>
<td></td>
<td></td>
<td>c: In-transit metastases/satellites without metastatic nodes</td>
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<tr>
<td>N3</td>
<td>4+</td>
<td>a: Micrometastasis(^a)</td>
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<td>b: Micrometastasis(^b)</td>
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**Distant metastases (M)**

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<tr>
<th>Site</th>
<th>Serum LDH</th>
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<tbody>
<tr>
<td>M0</td>
<td>NA</td>
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<tr>
<td>M1a</td>
<td>Normal</td>
</tr>
<tr>
<td>M1b</td>
<td>Normal</td>
</tr>
<tr>
<td>M1c</td>
<td>Elevated</td>
</tr>
<tr>
<td>Clinical Stage</td>
<td>T1a</td>
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<tr>
<td>IA</td>
<td></td>
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<tr>
<td>IB</td>
<td>T1b</td>
</tr>
<tr>
<td></td>
<td>T2a</td>
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<tr>
<td>II A</td>
<td>T2b</td>
</tr>
<tr>
<td></td>
<td>T3a</td>
</tr>
<tr>
<td>II B</td>
<td>T3b</td>
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<td>T4a</td>
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<tr>
<td>II C</td>
<td>T4b</td>
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<td>III</td>
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* Clinical staging includes microstaging of the primary melanoma and clinical/radiologic evaluation for metastases. By convention, it should be used after complete excision of the primary melanoma with clinical assessment for regional and distant metastases.

+ Pathologic staging includes microstaging of the primary melanoma and pathologic information about the regional lymph nodes after partial or complete lymphadenectomy. Pathologic Stage 0 or Stage IA patients are the exception; they do not require pathologic evaluation of their lymph nodes.
SURVIVAL

- **Stage IA:** The 5-year survival rate is around 97%. The 10-year survival is around 95%.
- **Stage IB:** The 5-year survival rate is around 92%. The 10-year survival is around 86%.
- **Stage IIA:** The 5-year survival rate is around 81%. The 10-year survival is around 67%.
- **Stage IIB:** The 5-year survival rate is around 70%. The 10-year survival is around 57%.
- **Stage IIC:** The 5-year survival rate is around 53%. The 10-year survival is around 40%.
- **Stage IIIA:** The 5-year survival rate is around 78%. The 10-year survival is around 68%.
- **Stage IIIB:** The 5-year survival rate is around 59%. The 10-year survival is around 43%.
- **Stage IIIC:** The 5-year survival rate is around 40%. The 10-year survival is around 24%.
- **Stage IV:** The 5-year survival rate is about 15% to 20%. The 10-year survival is about 10% to 15%. The outlook is better if the spread is only to distant parts of the skin or distant lymph nodes rather than to other organs, and if the blood level of lactate dehydrogenase (LDH) is normal.
MANAGEMENT IN EVOLUTION

- 1991 – World Health Organization Melanoma Study
  - Wide local excision with 1cm vs. 3cm margin for tumors less than 2mm in thickness
  - All local recurrence occurred in patients with tumors between 1-2mm in thickness with a 1cm resection margin
  - No difference in overall survival
- Intergroup Melanoma Trial
  - Compared 2cm vs. 4cm margins for tumors 1-4mm thick
  - Recurrence was the same between groups
- Swedish Melanoma Trial and French Melanoma Trials
  - Compared 2cm vs. 5cm margins for tumors less than 2mm in thickness
  - No significant difference in disease-free or overall survival between groups
BIOPSY MARGINS

- Lesions with a thickness up to 1mm – 1cm margin
- Lesions with thickness 1-2 mm – 1-2 cm margins (slightly higher local recurrence but no overall survival difference if tissue sparing required)
- Lesions with a thickness above 2mm – 2cm margin

- Subungual melanomas are treated with amputation of the distal digit to provide a 1cm margin; usually involves only the distal phalanx
- Large lesions on the face/neck may require tissue-sparing biopsy
LYMPH NODE EVALUATION

- 1800s - Lines of Sappey (L2 across the iliac crest to umbilicus)
- 1970s – Morton described lymphscintigraphy using technetium 99m-labeled colloid which was inject intradermally at the primary site
- 1980s – Morton injected blue dye intradermally at the primary site drained to the Sentinel Lymph node
- Wounds are also be palpated since nodes obliterated with tumor may not take up dye or radioisotope
SENTINEL LYMPH NODE BIOPSY

- Studies show lower rates of in-basin recurrence after SLNB compared with TLND; 2-10% vs. 20-50%; suggests that early treatment of regional lymph node metastases promotes regional control
- Preoperative lymphoscintigraphy offers an individualized “road map” of nodal basin drainage
- What to do with a positive SLNB remains controversial
SENTINEL LYMPH NODE BIOPSY

- Multicenter Selective Lymphadenectomy Trial-1 (MSLT-1)
  - 1269 patients with primary melanoma >1mm
  - Randomized for either (a) SLNB with completion LN dissection if positive or (b) nodal observation and therapeutic lymph node dissection for palpable lymphadenopathy
  - Primary endpoint was melanoma-specific survival
  - Results:
    - No significant melanoma-specific survival at 5 years (87% for both groups)
    - Small benefit in disease-free survival at 5 years with group A (78% vs 73%)

- MSLT-2: prospective randomized trial comparing SLNB with completion LN dissection versus observation only; primary endpoint is melanoma-specific survival
SENTINEL LYMPH NODE BIOPSY

- Survival benefit to patients with positive sentinel node melanoma after completion lymph node dissection may be limited to the subgroup with a primary lesion Breslow thickness greater than 1.0 and less than or equal to 4mm (pT2-pT3).
  - N = 544
  - Randomized prospective review
  - SLNB with completion LN dissection vs. therapeutic LN dissection
  - Statistically significant OS benefit for the group undergoing SLNB with CLND at 5 years (57.2% versus 37.9%) in the subgroup of patients with Breslow thickness 1-4mm

Annal Surg Oncol 2008 Aug;15(8) 2223-34
www.downstatesurgery.org
SLNB should be considered in higher risk stage 1B (thickness >0.75mm, positive deep margins, lymphovascular invasion)

SLNB should be offered in stage II melanoma patients

Consider complete LN dissection in stage III if SLNB is positive or clinically positive nodes

SLNB should be considered if primary melanomas were inappropriately diagnosed with shave biopsy and cauterized or underwent cryotherapy
ADJUVANT THERAPY AND TRIALS

- Hyperthermic arterial limb perfusion with melphalan
  - Alkylating agent used to treat multiple myeloma, ovarian cancer, malignant melanoma
  - Considered for patients with multiple in-transit metastases
- Interferon alfa-2b
  - Prolonged relapse-free survival and overall survival not reproducible
- Vermurafenib, dacarbazine
- Radiation therapy has been recommended for head/neck melanomas and mucosal melanomas in the pelvic region
- Intrallesional BCG vaccine
POSTOPERATIVE MONITORING

- Physical examination is the most important aspect of the return visit
  - 3-6 month intervals until 3-5 years from surgery (75% of all recurrences)
  - LDH
  - Complete skin examination
  - Evaluation for lymphadenopathy
  - CXR, Head CT and PET-CT
MELANOMA IN PREGNANCY

• Reports suggest adverse relationship between pregnancy and outcome in melanoma.

• Recommendation is for early termination and delaying next pregnancy for 2 years after treatment.
SYNOPSIS

- Melanoma is clinically diagnosed with a detailed history and physical examination.
- Tissue biopsy will provide histological diagnosis and predictors of survival.
- Wide local excision is the preferred treatment for all suspicious pigmented lesions.
- PET-CT, lymphoscintigraphy and blue dye provide preoperative and operative localization of sentinel lymph nodes.
- Lymph node dissection remains controversial given the morbidity of the procedure. Multiple prospective studies have demonstrated that decreasing microscopic tumor burden there is evidence of preventing further spread in a select group of patients.
- SLNB is suggested for stages 1B-IIA/B.
- Completion LN dissection is suggested for stages III A/B.
Questions?