Head and Neck Melanoma: Management of Neck Nodes

GBMC Head and Neck Grand Rounds
The Milton J. Dance, Jr. Head & Neck Center
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GBMC Grand Rounds: Case Presentation

Babar Sultan MD
10/3/08
74 yo M, several months prior to 11/07 noted lesion on top of scalp. Patient has had many basal cell carcinomas in past including left ear. Lesion not dark in color.

Biopsy by dermatologist: nodular malignant melanoma: 1.4 mm depth, no ulceration, Clark Level IV
RM

- **PMH:** h/o Basal Cell, hypercholesterolemia
- **PSH:** hernia repair, right knee replacement, hemorrhoidectomy, detached retina repair
- **SH:** Quit smoking forty years ago (15 pack year), mod user of alcohol, no h/o radiation exposure
- **FH:** No h/o melanoma, Father died of colon cancer, mother of natural causes, Brother has pancreatic cancer
RM

- PE: Vertex of scalp, 1.9 cm transverse scar.
- Palpation, U/S: No neck lymphadenopathy
Underwent PET/CT scan: small focus of uptake along the site of biopsy, no distant metastasis

11/15/07: WLE, STSG, excision sentinel node in postauricular region

Node: metastatic malignant melanoma

2/08: Left neck dissection Levels 2, 3, 5, occipital exploration, partial lower parotidectomy: All nodes negative
8/08: Patient returned for clinic visit. Dermatologist biopsied lesion anterior and to right of his melanoma site on scalp: malignant melanoma: 2.2 mm deep

On PE: dermal thickening and nodularity seen near skin graft site

Biopsy: malignant melanoma
Repeat PET/CT: Multiple pulmonary metastasis as well as retroperitoneal lymph node
Consult Medical Oncology
PET/CT from 10/07 showing only the single scalp lesion
Axial PET/CT Images from 2008 showing new scalp lesions
Axial PET/CT images 2008 showing new lung metastases
Axial PET/CT Images showing subcutaneous metastasis overlying the right back musculature
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Outline

- Review of clinical melanoma
- Staging
- Excision Margins
- Role of Sentinel Node Biopsy
- Role of Neck Dissection
- Is H+N melanoma a separate entity?
Clinical Presentation

- Malignancy of melanocytes, located predominantly in the skin, but also found in eyes, ears, GI tract, leptomeninges, oral and genital mucosa.

- 4% of skin cancers – 74% of skin cancer deaths

- Incidence: tripled in Caucasian population past 20 years, now sixth most common cancer.
  - Lifetime incidence is 1 in 60 for Caucasians
  - Highest incidence in Australia and New Zealand.
Clinical Presentation cont.

- Clinical: New or changing mole or blemish. Bleeding, itching, ulceration

- The “ABCDE” criteria
  - Asymmetry
  - Border irregularity
  - Color variegation
  - Diameter (> 6mm)
  - Evolving
Risk Factors

- **Etiology** - sites of intermittent, intense sun exposure
  - Fair-complexion
  - Residence near equator
  - Blistering sunburns in childhood and adolescence

- **Age** - median age is 53
  - Most common cancer in women age 25-29, second only to breast cancer in women age 30-34
Race and Melanoma

Disease effects primarily Caucasians
- African Americans incidence 1/20\textsuperscript{th}
- Hispanic incidence 1/6\textsuperscript{th}
Staging

- AJCC revised staging system from 2002
- Uses Breslow depth instead of Clark’s Level except for IA and IB
- Ulceration is a significantly negative predictor
- Staging validated in 17,000 patient study
- See Handout
Validated Survival Curve
Surgical Margins

- Melanoma in situ – 5mm
- <1.0 mm – 1 cm
- 1-2 mm – 1 cm
- 1 – 4 mm – 2 cm
- >4 mm – 2 cm
Surgical Margins

- **Intergroup Melanoma Surgical Trial (Balch et al)**
  - Began in 1983
  - Goal to examine optimal surgical margins for melanoma 1-4 mm thick.
    - Trunk + extremity randomized to 2 or 4 cm margins.
    - H+N given 2 cm margins.
  - No difference in local recurrence between 2 or 4 cm margins
  - Local Recurrence by site:
    - H+N – 9.4%
    - Proximal extremity – 1.1%
    - Trunk - 3.1%
    - Distal extremity - 5.3%
  - 5 year survival only 9% if local recurrence compared to 86% if no evidence of local disease
Surgical Decision Making

- Intermediate thickness melanoma have known rate of lymph node recurrence / involvement (15-20%)
- Should all patients have comprehensive node dissections?
- Should all patients be observed for clinical evidence of nodal involvement?
- Can sentinel node biopsy improve outcomes vs. either of these two options?
  - If node is positive, what surgical procedure should be performed?
Elective Lymph Node Dissection

- Comprehensive dissection of lymph nodes assumed to drain primary tumor
  - Advantages:
    - Poor outcomes when clinical nodes are detected
  - Disadvantages:
    - Unpredictable nature of drainage patterns
    - 80-85% of patients undergo unnecessary surgery
Evidence

- Intergroup Melanoma Trial (Balch)
  - Randomized trial, 10 year followup – Elective lymph node dissection vs. ‘Watch and wait’
  - Combined analysis with of H+N with truncal melanoma – no survival difference between groups

- 3 of 10 cohort studies show survival benefit for ELND vs WW
  - Lower depth cut-off 1.0-1.5mm, upper limit 3.0-4.0mm
Watch and Wait

- Standard practice for thin melanoma (<1 mm)
- Requires rigorous followup
- Ultrasound is used for more sensitive detection of nodes
  - Small subgroup will have surgery earlier than detected by other methods
  - Survival advantage not clear
Sentinel Lymph Node

- Receives lymph directly from primary melanoma, if free of disease, other nodes in basin will also be free of disease
  - 10% rule – used to determine sentinel node’s’
- Duel tracer results in higher identification rates
  - Temporal variation in lymphatic flow
- Most important prognostic indicator for long-term survival
Evidence

- Multicenter Selective Lymphadenectomy Trial (MSLT)
  - 1347 patients randomized to sentinel node biopsy or observation – if node positive then complete lymphadenectomy
  - Melanoma between 1.2 to 3.5 mm
  - Vital blue dye, radiocolloid
Disease free survival improved, but this is inherent in the study design, because of expected relapse in watch and wait group

- 78/500 (15.6%) patients in observation group had node relapse
- 122/764 (16.0%) of sentinel nodes were positive
  - False negative rate 26/764 (3.6%)

Subgroup Analysis: 12% absolute risk reduction in melanoma-specific mortality comparing sentinel-node positive patients (including false negatives) vs. node positive in observation group

- 66% vs 54%
Management After Positive Sentinel Node

- Multicenter Selective Lymphadenectomy Trial-2
  - Ongoing and recruiting study
  - Randomizing patients with positive sentinel-node to observation or completion lymphadenectomy

- Positive nodes found in about 15% of patients (range from 9% to 42%), even less clear if micro-metastases found have clinical significance
Sunbelt Melanoma Trial

- 79 center trial, goal of 3600 patients
- Dual goals
  - Evaluate prognostic / surgical significance of micromets detected by PCR in sentinel lymph nodes
  - Evaluate value of systemic Interferon treatment for localized melanoma
Results of Sunbelt

- Not yet published, presented at ASCO
- 64 month followup
- No difference in DFS or OS in either Protocol A or Protocol B

Conclusions:
- Interferon does not improve survival in non-disseminated melanoma
- Interventions for nodes positive by RT-PCR offers no survival benefit over observation either by lymphadenectomy nor lymphadenectomy + Interferon
Is H+N Melanoma a Separate Entity?

- Unique sun exposure
- Rich and complex lymphatic drainage
  - Anatomic predictions of nodal drainage basins is poor
- Most studies confirm increased likelihood of recurrence and diminished overall survival

- Can evidence from larger clinical trials be applied to H+N melanoma?
John Wayne Cancer Center

- 773 patients with tumor negative sentinel lymph node
  - 8.9% developed recurrence
- Multivariate analysis
  - Tumor thickness, ulceration
  - Location on H+N
  - All significant for decreased DFS
Sunbelt Melanoma Trial

- Higher number of SLN per nodal basin
  - 2.8, 2.7, 2.1 for H+N, trunk, extremity
- Higher false negative rates
  - 1.5% vs. 0.5% (p<0.05)
- Fewer histologically positive nodes despite similar Breslow thickness and presence of ulceration
  - 15% vs 23.4% and 19.5% (p<0.001)
- Nodes less likely to contain blue dye
Population Databases

- **SEER**: 5 and 10 year survival worse for scalp/neck compared to extremity, trunk, face
  - 51,704 non-Hispanic white adults

- **German Database**: No difference in overall survival for H+N vs other sites
  - 5702 patients
Conclusions

- No evidence to support comprehensive lymph node dissection in all patients
- Sentinel lymph node biopsy and subsequent lymph node dissection may improve outcomes in those with positive nodes, but not in all patients
- Aggressive treatment of micromets does not result in superior survival outcomes
- Sentinel node biopsy is technically and anatomically more challenging in H+N melanoma
- Population studies may indicate that H+N melanoma is a distinct entity with worse outcomes