Melanoma-Back to Basics…

I Thought I Knew Ya!

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At tumor board, a surgeon insists that all level II melanomas are invasive since they have broken through the basement membrane. Your appropriate reply is...

A. I Agree
B. I Disagree
C. It depends upon the body site
D. Level II melanomas do not exist
Histopathological Parameters

Breslow Thickness

Melanoma

Clark’s Level

Vertical/Radial Growth Phase
# Growth Phase

<table>
<thead>
<tr>
<th>Vertical growth phase (VGP)</th>
<th>Potential to metastasize</th>
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<tr>
<td>Radial growth phase (RGP)</td>
<td>Believed to lack competence for metastasis</td>
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Clark’s Levels

I - ?
II - Papillary Dermis
III - Filling papillary dermis
IV - Reticular Dermis
V - Subq fat

Eliminated in AJCC 2002
What Invasion IS

- Expansile nests within the dermis
- Clearly different cytology compared to junctional component
- Mitotic figures
What Invasion ISN’T

- Melanocytes in the papillary dermis
- Level II
Caveats

- Re-review of three cases with metastasis of RGP melanomas were re-reviewed
- Deeper sectioning revealed a focus of vertical growth in one case
- In the other two cases, only radial growth was found
  - One case with regressive changes
  - One case with adjacent compound nevus with periadnexal involvement
- CONCLUSIONS
  - True RGP melanomas have an excellent prognosis
  - Possible that strictly defined RGP melanomas may metastasize in very rare cases
  - Caution must be exercised in defining a lesion as having no metastatic potential when:
    - Multiple sections of the primary lesion are unavailable
    - Regressive changes
    - Associated melanocytic nevus

Caveats

- Retrospective, multicenter, and case-control type study
- Vertical growth phase is the only statistically significant prognostic factor for thin level II cutaneous SSM
- Conclusions
  - Growth phase evaluation should be added to the recommendations for melanoma histologic report, at least for level II SSM
  - Minimum of eight serial sections mandatory not to underdiagnose vertical growth phase

Melanoma in Papillary Dermis

- Non-Invasive Radial Growth Phase
- Vertical Invasive Growth Phase
- Regression
Measuring the Melanoma

- Measure from granular layer to the deepest extent of the dermal component
- Measure at right angles to surface of skin above tumor, avoid tangential sections
- Avoid hair follicles/adnexal structures
  - Atypical melanocytes in a column perpendicular to the epidermis are probably periappendageal
- Take at least 3 measurements
Special Situations

- Arising with pre-existing melanocytic nevus
- Prior biopsy or excision
- Ulceration
- Epidermal thickness
- Polypoid melanomas
- Verrucous melanomas
- Perineural invasion
- Mucosal melanomas
- Melanomas in soft tissue
Melanoma Arising with Nevus

- Morphology
- "p53, Ki67"
Prior Biopsy or Excision

- Depths are not additive
- Measure melanoma away from prior biopsy site
Ulceration

- Measure from base of ulcer to deepest dermal invasion
- Disclaimer that measurement may underestimate true thickness
Epidermal Thickness

- Melanomas of acral skin may have epidermal hyperplasia twice as thick as non-acral skin.
- If epidermis is thickened, should note that much of measured thickness is due to epidermal hyperplasia.
Polypoid Melanomas

- Clark’s levels break down
- Measure thickness
- Consider multiple measurements
Verrucous Melanomas

- Take an average of peak to trough
- Report maximal, minimal, and mean
Perineural Invasion

- If melanoma involves the nerve, measurement should include the deepest involved nerve.
Mucosal Melanomas

- Overall poor prognosis
- Always rule out metastasis
- 37 patients H/N oral mucosa MM
  - 35 surgical resection/2 radiotherapy
  - Twenty-six were dead at follow-up
  - Twenty-one of them died of disease
  - Median survival, 2.4 years
- No prognostic significance was found for tumor thickness, level of invasion, ulceration, mitotic index, or nerve/nerve sheath involvement

Melanomas of Soft Tissue

- Metastasis
- Clear cell sarcoma
- True soft tissue melanoma
  - Current AJCC staging classification, these tumors are considered Stage IV disease (metastatic melanoma with an unknown primary)
  - 11/1800 patients were identified (0.61%) with a single focus of presumed metastatic disease
  - Kaplan-Meier 8 year survival curve was 83%
  - Possible these presumed metastatic tumors do not behave like stage IV metastatic disease to the skin but instead behave as primary tumors

Arch Dermatol 2000;136:1397-1399
Important Histopathologic Parameters

- Depth of invasion
- Ulceration
- Lymphovascular invasion
- Margins
- Regression
Melanoma Frozen Section Margins

- Dermatopathologists (15) compared en face frozen sections compared with standard paraffin-embedded sections.
- 2 sets of lesions: malignant melanomas (MMs) and 10 from nonmelanocytic lesions (NMLs) randomly.
- Of 330 evaluations, there were 132 diagnostic discrepancies (40.0%).

*Am J Clin Pathol 2003;120:203-208*
Melanoma Frozen Section Margins

- 66 each for MM and NML (mean per case for both diagnoses, 6)
  - In 9 instances (6.8%), the change was from positive (frozen) to negative (permanent) and in 43 (32.6%), from negative (frozen) to positive (permanent)
  - Poor agreement between frozen and permanent sections

- Conclusions:
  Permanent histology is "gold standard" for histologic evaluation
  En face frozen sections **not** suitable for accurate surgical margin assessment of melanocytic lesions
Regression

- Measure to deepest extent
- Consider bleach with MART1/S100
- Add disclaimer that it may represent an underestimation of the true biological potential of the melanoma
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Questions

If confusion is the first step to knowledge, I must be a genius.

Larry Leissner