R/O BCC

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Clinical Information

- 74 y.o. man with lesion on left side of neck
- r/o BCC
Desmoplastic Melanoma
What is your diagnosis?

1. SCCis + neurofibroma
2. invasive SCC, spindle cell type
3. SCCis + desmoplastic melanoma
4. SCCis + sclerotic fibroma
5. other

The Excision
Desmoplastic Melanoma

What is your diagnosis?

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S100-protein
Desmoplastic Melanoma

Definition
- spindle cell melanoma
  - composed of spindled melanocytes
- desmoplastic melanoma
  - prominent desmoplastic component
- combined desmoplastic melanoma
  - ordinary melanoma with focal desmoplasia
  - neurotropic melanoma
  - prominent perineural growth and invasion

Desmoplastic Malignant Melanoma
- first described by Conley et al. in 1971
- a) spindle cell proliferation, composed of single cells or at most small aggregates of 2-3 cells, separated by abundant collagen
- b) cytologic atypia of spindle cells
- c) atypical junctional melanocytic proliferation
- d) neurotropism - invasion of endoneurium or perineurium
- e) neuroma-like differentiation

Diagnosis
- Squamous cell carcinoma in situ over desmoplastic melanoma
Desmoplastic Melanoma

**Frequency**
- uncommon
  - <4% of melanomas seen at Sydney Melanoma Unit
  - <2% of melanomas seen at Memorial Sloan-Kettering Cancer Center

**Clinical Parameters**
- slight male predominance (1.3 : 1)
- mean age at presentation: 63 years (46 yrs. for other melanomas)
- can affect people at any age, including teenagers

**Clinical Parameters**
- location:
  - head/ neck
  - trunk
  - extremities
  - mucosa
  - volar/ subungual sites

**Arising in conjunction with**
- lentigo maligna
- acrolentiginous melanoma
- mucosal melanoma
- de novo

**Clinical Presentation**
- painless amelanotic nodule
- occasionally: indurated or depressed plaques
- scar
- 0.5 - 6.0 cm
- neuralgia or paresis in neurotropic melanomas
Desmoplastic Melanoma

Clinical Parameters
- Patients present at later stage of disease
  - 28% are AJCC Stage I vs. 80% for other melanomas
  - Median thickness at presentation 2.5mm-4mm vs. 1.0 mm for other melanomas
  - >90% are Clark’s level IV or V at presentation

Delay of diagnosis
- Clinical recognition difficult
  - Scarlike nodule, no hx of trauma
  - Often not pigmented
  - Misdiagnosed as scar, basal cell carcinoma, cyst, dermatofibroma
  - Bland histology, resembling fibrohistiocytic proliferation
  - Superficial/partial biopsies

Histology
- Overlying intraepidermal component present in about 3/4 of cases
- Tumors without intraepidermal component are generally thicker
- Absence of intraepidermal component
  - Regression
  - Ulceration
  - Trauma/LN2
Desmoplastic Melanoma

Histologic Spectrum
- significant variability in
  - cellular density
  - cytology
- scar-like DM → spindle cell melanoma

Architecture for pure DM
- pink tumor
- ill-defined tumor margins
- lymphoid aggregates
- desmoplasia
- myxoid stroma
- invasion of perineurium
- invasion of endoneurium
Desmoplastic Melanoma

Cytology for pure DM

- reminiscent of neurofibroma
- spindle cells with elongated, wavy nucleus
- focal pleomorphism
- melanin scant (44-73% amelanotic)
- mitotic activity variable
Desmoplastic Melanoma
Desmoplastic Melanoma

Which antibody stain is most sensitive for desmoplastic melanoma?

1. HMB-45
2. Melan-A
3. MITF
4. S-100 protein
5. tyrosinase

Immunohistochemistry

- S100-protein+
- vimentin -
- HMB-45 -
- keratin -
- Leu7 -
- SMA+
- Desmin -
- CD68 (KP1) weak and focal

S100-protein

- positive in 90-95% of desmoplastic mm
- nearly 100% positive in spindle cell mm
- nuclear and cytoplasmic staining
- usually strong and diffuse, but can be focal and weak
- beware! dermal Langerhans' and dendritic cells
Desmoplastic Melanoma

**HMB-45, Mart-1, Tyrosinase, gp100, MTP**
- more specific than S100
- virtually never positive in purely desmoplastic mm
- positive in spindle cell mm, or desmoplastic mm with spindle cell component
- correlates with amelanotic nature (marker of pre-melanosomes)
- can be useful in DD with blue nevus

**Smooth Muscle Actin**
- positive in 1/3 of desmoplastic mm
- number of actin positive spindle cells may equal number of S100 positive cells
- probably reactive myofibroblasts

**Immunohistochemistry - Summary(1)**
- Immunohistochemical profile of desmoplastic mm differs from ordinary mm
- S100-protein is the most sensitive stain for desmoplastic mm

**Immunohistochemistry - Summary(2)**
- S100-protein negative cases occur and do not rule out the possibility of desmoplastic melanoma in the presence of other supporting evidence
- melanocytic differentiation markers not helpful in diagnosis
- Actin positive spindle cells can be present in significant numbers

**The most likely adverse event for a desmoplastic melanoma (3mm) is:**
1. metastasis to local lymph node (SLN) 33%
2. distant metastasis 33%
3. local recurrence 33%

**Definition of DM**
- most studies lack precise inclusion criteria
- strict definition paramount because of implications for outcome
- MSKCC criteria (Klaus Busam):
  - DM: >= 90% of invasive tumor paucicellular desmoplastic
  - combined DM: <90% desmoplastic and paucicellular
Desmoplastic Melanoma

Prognosis (historical)

- Overall survival at 5yrs: 68%/75.2%
- Overall survival rate is lower than for other melanomas
- Stage for stage survival is better than for other melanomas
- Data needs to be interpreted with caution because of lack of uniformity in definition of DM

Prognosis (historical)

- 11-49% local recurrence rate vs. 3.2% for other melanomas
- Local recurrence earlier than in other melanomas
- Local recurrence associated with margins < 1cm
- Local recurrence higher for neurotropic desmoplastic mm
- Lower incidence of LN metastasis

Prognosis of pure DM

<table>
<thead>
<tr>
<th>Type</th>
<th># patients</th>
<th>Local recurrence</th>
<th>Regional LN</th>
<th>Distant</th>
</tr>
</thead>
<tbody>
<tr>
<td>pure desmoplastic</td>
<td>67</td>
<td>5(7%)</td>
<td>1(1%)*</td>
<td>7(10%)</td>
</tr>
<tr>
<td>mixed</td>
<td>21</td>
<td>1(5%)</td>
<td>2(10%)</td>
<td>5(24%)</td>
</tr>
<tr>
<td>conventional</td>
<td>1973</td>
<td>43(2%)</td>
<td>123(6%)</td>
<td>212(11%)</td>
</tr>
</tbody>
</table>

1 patient with LN met also had lung metastases

Similar MSM, despite 2-fold difference in Breslow depth

Melanoma specific mortality
Desmoplastic Melanoma
Desmoplastic Melanoma

Prognostic Factors
- high mitotic rate
- thickness
- composition of tumor: desmoplastic vs. mixed

Metastases
- desmoplastic
- spindled
- conventional

Differential Diagnosis
- scar
- fibrous histiocytoma
- atypical fibroxanthoma
- benign and malignant nerve sheath tumors
- leiomyoma/ leiomyosarcoma
- spindle cell carcinoma
- DFSP
- spindle cell nevus

<table>
<thead>
<tr>
<th>Criterion</th>
<th>Desmoplastic mm</th>
<th>Desmoplastic Nevus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Margins</td>
<td>poorly circumscribed</td>
<td>inverted wedge</td>
</tr>
<tr>
<td>Atypia</td>
<td>present</td>
<td>absent</td>
</tr>
<tr>
<td>Mitoses</td>
<td>present</td>
<td>absent/ rare</td>
</tr>
<tr>
<td>Maturation</td>
<td>absent</td>
<td>present</td>
</tr>
<tr>
<td>Neurotropism</td>
<td>present</td>
<td>absent</td>
</tr>
<tr>
<td>Lymphocytes</td>
<td>follicles</td>
<td>scant</td>
</tr>
<tr>
<td>IPOX</td>
<td>HMB-45, Mart-1: -</td>
<td>HMB-45, Mart-1: +/-</td>
</tr>
</tbody>
</table>
Histologic clues to diagnosis

- remember desmoplastic melanoma in your DD
- atypical junctional melanocytic proliferation
- lymphoid follicles
- neurotropism
- neuroma-like differentiation
- myxoid change in dermis
- dermal melanin

Summary Desmoplastic MM (1)

- one of the most treacherous diagnoses in pathology
- figures in differential diagnosis of nearly every dermal spindle cell proliferation
- Immunophenotyping paramount in evaluation of dermal spindle cell proliferations

Summary Desmoplastic MM (2)

- depth for depth better prognosis than ordinary melanoma
- poor survival statistics because of high stage at time of presentation
- separation into pure DM and mixed DM important
- SLN biopsy of questionable utility for pure DM