Desmoplastic Malignant Melanoma

- Arise most often in setting of chronically sun-exposed skin
- Patients usually aged 60 and over; head and neck most common
- Painless indurated plaque or scar-like thickening; some begin as small papule or nodule
- Pigmentation usually related to associated lentigo maligna
Desmoplastic Melanoma - Microscopic

- Dermal spindle cell proliferation, resembling fibroblasts with varying degrees of atypia and usually non-pigmented
- Embedded in fibrous or fibromyxoid stroma
- Lymphocytic aggregates
- Sometimes neuritropism, or formation of nerve-like structures
- Junctional changes minimal to absent in ½ of cases; can be features of lentigo maligna
- May be "pure" (> 90%) desmoplastic or mixed with non-desmoplastic foci
- IHC positive for S100, SOX10, NGFR; negative for melanosome markers except in combined types
Desmoplastic Malignant Melanoma

- Typical clinical setting
- Frequent junctional changes
- Lack of symmetry
- Lack of maturation
- Mitoses
- Prominent lymphocytic infiltrate
- Immunohistochemistry

Desmoplastic Malignant Melanoma – Differential Dx

- Desmoplastic Spitz nevus
- Sclerosing cellular blue nevi (diffusely HMB45+)
- Immature scars
- Dermatofibroma, atypical fibroxanthoma, sarcomatoid carcinoma, leiomyosarcoma
- Neurofibroma (Husain and Silvers, J Cutan Pathol, 2013)
Desmoplastic Malignant Melanoma - Prognosis

- High recurrence rate
  - Neurotropism may play a role here, as well as diagnostic problems
- Up to 1/3 of these lesions metastasize
- Behave more like sarcoma; regional lymph node involvement less common (especially in “pure” desmoplastic melanomas)

16

17

18
Unusual Melanocytic Tumors

1. Squamo-melanocytic tumor
2. Neurocristic hamartoma

Squamo-Melanocytic Tumor

- Reported in 1999 by Pool, Manceii, Clark and Harrist
- Purple-black nodule on face of middle-aged or older persons
- Recurrence, metastasis not reported; however, outcome of other, non-reported cases is uncertain

Squamo-Melanocytic Tumor

- Atypical epithelial cells with admixed epithelioid to spindled cells and pigment production.
- Atypical keratinocytes are cytokeratin positive; melanocytes express S100 and HMB45
Squamo-Melanocytic Tumor

- An 83 year old man underwent FNA of a cervical lymph node, showing melanoma
- Biopsy of preauricular skin showed these changes:
- Parotidectomy showed metastatic melanoma in intraparotid node

Cytokeratin

S100
Neurocristic Hamartoma

- Controversial “entity”
- Relationships to patch and plaque-like blue nevi
- “Schwannian” elements may represent differentiation within a nevus rather than composite tumor
- Variant: pilar neurocristic hamartoma
- Relationship to “animal melanoma”
Metastatic Melanoma

- Skin is most common site of melanoma metastasis (56%)
- Local, regional, or distant extension by lymphatic, hematogenous, angiotropism, or perineural routes
- One study: 8.3% of patients presented with skin metastasis as only manifestation of disease
- Leg>scalp>arm>face

Metastatic Melanoma

- Solitary pigmented nodule most common, but also zosteriform, blue nevus-like, erysipelas-like, sclerodermiform, purpuric lesions
- Satellite metastasis: within 2 cm of primary site
- In-transit metastasis: >2cm from primary site but not reaching ipsilateral regional lymph nodes
Metastatic Melanoma - Microscopic

- Well-circumscribed dermal nodule, composed of epithelioid cells, with little inflammation but surrounding fibrosis
- Epidermotropism in ≤ 5% of cases
- Angiolymphatic invasion in 5%
- Melanocytic differentiation indicated by fine cytoplasmic melanin granules

37

38

39
Metastatic Melanoma - IHC

- S100: highly sensitive but not specific
- Melan-A and HMB45: more specific but negative in ≤ 15% of metastatic melanoma cells
- Tyrosinase sensitive but staining may be seen in Schwann cells
- SOX10 highly sensitive, useful in distinguishing melanocytes from melanophages
- Ki-67 useful in nevoid cases
- PDL1 stain: may be helpful to assess for susceptibility to immune checkpoint blockade therapy

Metastatic Melanoma – Differentiation from Primary Melanoma

- Primary melanoma losing junctional component due to trauma or prior biopsy
- Primary dermal metastatic melanoma
  - Has lower levels of staining for p53, Ki-67, cyclin D1 than nodular or metastatic

Metastatic Melanoma – Differentiation from Primary Melanoma

- Epidermotropic metastatic melanoma
  - Dermal component broader than the junctional component favors metastatic
  - Accompanying benign nevus favors primary
  - Sheet-like growth, disturbance of surrounding stroma, mitotic activity
  - Elevated N:C ratio
Regression in Malignant Melanoma
Regression in Malignant Melanoma

- Three phases: inflammatory, reduction in tumor with early fibrosis; extensive fibrosis with telangiectasia
- Controversy regarding role in prognosis
- Extensive regression with involution of the primary tumor probably has adverse prognosis

Presentations of Completely Regressed Melanoma

- Vitiligo-like
- Lichenoid
- Tumoral melanosis
Desmoplastic Melanoma

“New” Markers:

- P75 nerve growth factor receptor
  - All spindle cell melanomas express in at least 10% of cells
- KBA.62 (recognizes an unknown antigen expressed by melanomas)
  - About ¾ stain with this marker; average of 39% of cells stain
- SOX10 (a transcription factor important in nervous system development)
  - In one study, strongly stained all desmoplastic melanomas
  - Less likely to stain fibrocytes and histiocytes
  - Its gene expression may be regulated by MiTF, but MiTF is weak or negative in desmoplastic melanomas

Plaza et al: Diagnostic Pathology

Performed an immunohistochemical analysis of desmoplastic melanoma using 14 antibodies; they conclude that a panel of S-100p, WT-1, SOX-10, p75 and nestin may be optimal for diagnosis

Stains

A: H&E; B: Nestin; C: WT-1; D: p16
Prame

• Preferentially Expressed Antigen in Melanoma
• Diffusely expressed in several types of melanoma (35% of desmoplastic melanomas)
• 86.4% of melanocytic nevi completely negative
  - Positivity seen – usually in a minor subpopulation – in 13.6% of common, traumatized, dysplastic, and Spitz nevi
Superficial Spreading Melanoma

HMB45

p16
Problems with Biopsies

- Thin shave biopsies are undesirable; small, partial biopsies may not be representative of the entire lesion
- Compression or crush may give false impression of maturation
- Tangential sectioning may give false impression of confluence
- Tissue artifacts
- Definitive diagnosis may not be possible
Conclusion

88