Immunohistochemistry of scarring processes - Landmines in IHC evaluation and use of multiplex antibodies

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Dr. Jukic has nothing to disclose.

What is the most feared scarring entity in dermatopathology?
- Keloid!
- Kaposi’s sarcoma
- Sclerosing Spitz’ nevus
- Desmoplastic melanoma
- Schwannian cell hyperplasia

MDeN: DIAGNOSTIC PITFALL
- For clinicians
  - In the absence of a prior history of melanoma, clinically not suspected until late
  - Typical submitted diagnoses: atypial, dermatofibroma, BCC, tar, keloid, other
  - Classically – there is a bewildered call from the clinical team: “Did you mix up the specimens?”

Melanoma Desmoplasticum et Neurotropicum
- ...melanoma which elicits the production of abundant collagen” (Conley et al. 1972)
- “fibrous tumor whose individual spindle cells are isolated in a dense fibrous matrix” (Reed and Leonard 1979)
- “collagenizing fibrosarcoma-like” melanoma (Jain and Allen 1989)
More issues with MDeN

- Benign process oversight
- Malignant oversight
- Melanocytic oversight

Immunohistochemistry, as the legends would have it

- “Old” antibodies
  - Strongly positive for S-100, NSE, CD56, and NGFIR
  - Negative for other “melanocytic” differentiation markers
  - Negative for epithelial markers
  - May be positive for collagen type IV, laminin, FXIIIa, SMA

- Desmoplastic melanoma
  - Sox 10
  - Nestin
  - Wt-1

Other things to remember

- Rare variant (< 4% of melanomas)
- Predominantly affects the head and neck region of patients with chronic sun damage
- Often associated with lentigo maligna
- Often presents as a deep lesion
- High rate of local recurrences
- Regional lymph node involvement less common than in patients with conventional melanoma

Ingrained adages

- First reported by J Conley, R Lattes, and W Orr MD (Cancer 1971)
- “...these tumors behave as highly malignant stubbornly recurring and often metastasizing neoplasms.”
  - Breslow thickness was not measured and no adjustments were made for this parameter when compared to conventional melanoma

Histological classification and prognosis

- Not all spindle cell melanomas are desmoplastic, albeit nearly all desmoplastic melanomas are spindle;
- Not all of the neurotropic melanomas are desmoplastic, albeit a high proportion of desmoplastic melanomas reveals neurotropism
- Combined melanomas are more common (conventional with a desmoplastic component)
- DMM has less frequent LN metastases; if they happen they exhibit conventional phenotype

Multiplex stain utility
Multiplex IHC antibodies to the rescue

- HMWK/Sox-10
- NGFR/HMWK
- NGFR/p63
- NGFR/Sox-10
- S100/HMWK
- p53/S100
- S100/ESA
- Tryosinase/Ki-67
- Melan-A/phH3
- S100/MCK

Multiplex stain comparison

In desmoplastic melanoma, antibodies usually do not cooperate;

This is a presentation of a classic case
Less Usual Presentation
Nodular subtype
Other nodular example
Summary so far

- Desmoplastic melanoma is an “ugly bugger”
- Looks worse than it behaves
- It might have better prognosis than some other melanomas if we match it Breslow for Breslow and Clark for Clark

Case from Sate Hamza, MD

A patient with a diagnosis of melanoma in situ from the cheek underwent an excision:

- https://www.flickr.com/photos/shamza/albums/72157661253035683
- Date: Nov, 2015
- Re-excision
- https://www.flickr.com/photos/shamza/albums/72157663410408142
- Dec 11, 2015
In summary ....

45 year old female Florida resident, veteran

- Underwent a “shave excision” of a nevus in 2012
  - Nevus diagnosed as lentiginous junctional Clark’s nevus with mild atypia
  - Margins free but close
  - Upper back

- Presents with pink scar with “rough surface”

- R/o recurrence
Case continued

- Scar with an increase in p75 and S100 positive cells, presumed dendrocytes
- Previous biopsy was pulled
- It was
  - Junctional nevus!!
  - Re-excision recommended

- Re-excision was received
87 year old gentleman, farmer

- Skin, left upper arm (near SCC scar), biopsy
- Pearly pink papule.
- The differential diagnosis includes basal cell carcinoma.
• Atypical basaloid growth with adjacent scar, laden with S-100 and p75 positive cells
• Differential diagnosis includes an early evolving desmoplastic melanoma and unusual Schwannian cell hyperplasia within the scar
Diagnostic option

- Schwann cell hyperplasia
- Unusual myofibroblastic proliferation
- Unusual nodular fasciitis like growth
- Evolving desmoplastic melanoma
- Peripheral nerve sheath tumor of some sort

Articles about p75 and Sox-10 positive cells

Are all “desmoplastic melanomas” indeed melanomas?

Peripheral nerve sheath tumor with overlying melanocytic hyperplasia?

- Minimal intraepidermal melanocytic hyperplasia
- The spindle cells in the dermis frequently in a nodular arrangement
- Better prognosis
- Quite a few patients are younger and have excellent prognosis
- Patient with NF-1

Schwann cell hyperplasia in the scar?

- Usually no melanocytic hyperplasia
- Cells within the scar a few and far between
- “Atypia is in the eye of beholder”
- “Better” cases I encountered
- Probably a related completely benign entity

It is a malignant peripheral nerve sheath tumor, it is not a desmoplastic melanoma

- Clarification:
  - “If you did not have a melanoma in situ overlying it, this is what you would have called it. At least I hope you would have!”
- Juan Rosai, MD