Update on Cutaneous Mesenchymal Tumors

Thomas Brenn
Cutaneous Mesenchymal Tumours

Wide morphological and biological spectrum

Myofibroblastic, smooth muscle, neural, vascular, adipocytic, undifferentiated; rare rhabdomyoblastic or osseous

Spindle cell, epithelioid, pleomorphic, vasoformative, fat forming

Benign to intermediate and high-grade malignant

Vast majority is benign

Distinctive behavior of malignant tumors presenting in the skin

High grade cutaneous sarcomas exceptionally rare
Case History

• 80 year-old male
• rapidly enlarging, crateriform nodule
• on the scalp
• clinical suspicion of keratoacanthoma or squamous cell carcinoma
• unremarkable past medical history
• diagnostic curettage was performed
Immunohistochemistry

NEGATIVE

- MNF116
- CK5/6
- AE1/3
- EMA
- P63
- Desmin

- S100
- Melan a
- CD31
- CD34
- ERG
Diagnosis:

Pleomorphic Dermal Sarcoma
Follow-up:

Negative Re-excision

Pulmonary metastasis 8 months after biopsy

Rapidly progressive disseminated disease

Patient died 12 months after biopsy
Pleomorphic Dermal Sarcoma

Closely related to AFX:

• Same clinical setting, similar clinical presenting features
• Similar histologic and immunohistochemical features
• Similar underlying genetic events

BUT

• Invasion of subcutis, tumor necrosis, LVI and PNI confer potential for aggressive behaviour
Pleomorphic Dermal Sarcoma

-Clinical Features-

- Sun-damaged skin
- Head and neck; scalp
- Elderly
- Strong male predilection
- Rapid growth
- Ulceration and bleeding
- 2.5 cm median

Pleomorphic Dermal Sarcoma
-Immunohistochemistry-

Diagnosis of exclusion

No positive discriminatory histological or immunohistochemical features

Consistently negative:
- S100
- multiple CK, especially HMW-CK
- Desmin
- CD34
Pleomorphic Dermal Sarcoma

-Genetics-

Frequent mutations in

- TP53 and TERT promoter
- FAT1
- NOTCH1/2
- CDKN2A
- But no difference AFX vs PDS

Pleomorphic Dermal Sarcoma

- Prognosis -

Risk for local recurrence (30%)
Metastasis (10-20%) to skin, soft tissue, Lung
Rare mortality (up to 20%)
Behavior likely more aggressive but f/u limited due to advanced age at presentation and significant co-morbidities

Pleomorphic Dermal Sarcoma

-Prognosis-

Presence of metastatic disease associated with high associated mortality (50%)

Pleomorphic Dermal Sarcoma

-Treatment-

Complete excision with negative margins

Consideration for adjuvant RTX if surgical clearance cannot be achieved

Clinical follow-up
Atypical Fibroxanthoma / PDS

Beware: Partial sampling, shave, curettage bx
Pleomorphic tumors on sun-damaged skin:

- Melanoma
- Poorly differentiated SCC
- Poorly differentiated angiosarcoma
- MPNST, DFSP, Leiomyosarcoma
Spindle Cell Squamous Cell Carcinoma
Spindle Cell Melanoma
Pleomorphic Dermal Sarcoma

Cutaneous Angiosarcoma

Cutaneous angiosarcoma:

- Significant clinical and morphological overlap
- Important distinction due to aggressive behaviour of cutaneous angiosarcoma
Pleomorphic Dermal Sarcoma

Cutaneous Angiosarcoma

CD31

Fli-1

CD31

Fli-1
Case History

- 81 year-old female
- Tumor on left arm
- ?SCC
CD10

S100

cytokeratin

Melan A
Diagnosis:

Atypical Fibroxanthomma?
Diagnosis:

Dedifferentiated (sarcomatoid) melanoma
Dedifferentiated melanoma

Collision tumour: atypical fibroxanthoma and invasive melanoma

Sir,
Atypical fibroxanthoma (AFX) and malignant melanoma presenting together as one combined cutaneous lesion (collision tumour) has only ever once previously been reported. This case report documents the second such case.

A 76-year-old male presented with a 17 mm diameter, ulcerated scalp nodule which had been growing over a period of 2–3 months. It was removed in a skin ellipse and a skin graft was performed. Histologically, the clinically presenting lesion was an ulcerated, pleomorphic, predominantly spindle cell proliferation extending into the subcutis, lying 1 mm from margins. It contained numerous atypical mitoses and scattered xanthomatised and giant/monster cells. Adjacent to one side of it and involving a side margin, within the papillary and upper reticular dermis, there was a blander, epithelioid tumour with an overlying lentigo maligna, representing invasive melanoma. Infrequent dermal mitoses were also seen within this component. There was melanin pigment within the epidermis adjacent to the larger lesion, which itself contained haemosiderin. No lymphovascular or perineural invasion (or neurotrophism) were seen (Fig. 1).

The availability of CD10 and PC1 as positive markers of AFX means it is no longer just a diagnosis of exclusion.

In the current case, the rapid growth of the AFX which over-ran the melanoma meant that the melanoma was diagnosed at early stage which should ensure a better prognosis for the patient.
Dedifferentiated melanoma

Desmoplastic Melanoma With Sarcomatoid Dedifferentiation

Maija Kiuru, MD, PhD,* Gregory McDermott, BA,* Michael Berger, PhD,*† Allan C. Halpern, MD,‡ and Klaus J. Busam, MD*
Desmoplastic Melanoma With Sarcomatoid Dedifferentiation

Maija Kiuru, MD, PhD,* Gregory McDermott, BA,° Michael Berger, PhD,°† Allan C. Halpern, MD,‡ and Klaus J. Busam, MD*

Abstract: Desmoplastic melanoma (DM) is a variant of melanoma, which typically affects chronically sun-damaged skin of elderly patients. Pure DM displays a low density of fusiform melanocytes in a collagen-rich matrix. In mixed DM, tumor cell density is higher, and parts of the tumor lack abundant stromal fibrosis. Both pure and mixed DMs usually express S100 protein homogeneously. We report herein an unusual biphenotypic tumor characterized by the association of a pure DM with an undifferentiated solid spindle cell nodule. It occurred on the scalp of a 66-year-old man. A biopsy of the undifferentiated spindle cell nodule was initially interpreted as a commercial laboratory as atypical fibroxanthoma. The pure DM was seen only in the excisional specimen. All cells of the pure DM stained for S100 protein and SOX10. The adjacent solid sarcomatoid spindle cell nodule lacked expression of S100 protein, SOX10, as well as melan-A, gp100, and microphthalmia-associated transcription factor in >95% of its tumor cells. Although focal expression of melanocyte differentiation antigens in the solid tumor component made us favor a combined DM with sarcomatoid dedifferentiation, we also considered the possibility of a collision scenario, that is, a pleomorphic dermal sarcoma incidentally colliding with a DM. To further assess a possible relationship of the sarcomatoid nodule with the DM, we performed next-generation sequencing analysis on each component separately. The analysis revealed shared chromosomal copy number changes and a high number of common mutations, thereby supporting the concept of a DM with a dedifferentiated sarcomatoid component. An interesting finding is the presence of mutations of the neurofibromin 1 (NF1) gene in both tumor components.

Key Words: desmoplastic melanoma, sarcoma, biphenotypic tumor, next-generation sequencing

Living on the Edge: Diagnosing Sarcomatoid Melanoma Using Histopathologic Cues at the Edge of a Dedifferentiated Tumor: A Report of 2 Cases and Review of the Literature

Emily M. Erstine, MD, MBA,* Michael T. Tetzlaff, MD, PhD,† Jennifer S. Ko, MD, PhD,* Victor G. Prieto, MD, PhD,† Alison L. Cheah, MBBS,‡ and Steven D. Billings, MD*

Abstract: Sarcomatoid melanoma is a rare type of melanoma lacking typical histologic features of melanoma and often lacks expression of S100 protein and melanocyte-specific markers. Given the rarity of this entity, its clinicopathologic findings are not well defined. We report 2 cases of sarcomatoid melanoma received in consultation: a 65-year-old woman with a right breast mass and a 62-year-old man with a left planar heel mass. Both lesions were ulcerated, pedunculated, highly cellular proliferations of atypical spindle cells arranged as fascicles and/or sheets. The tumor cells of the breast mass expressed CD10 and vimentin diffusely but S100 protein only focally. The tumor cells of the heel mass lacked expression of melanocytic markers altogether, except for weak, very focal S100 protein expression. At the junctional edge of the breast mass and in the ulcer base of the heel mass, focal precursor melanoma was present and exhibited melanocytic differentiation. We report these cases to emphasize the importance of meticulous histologic inspection at the lesion’s edge and/or ulcer base to correctly identify the conventional precursor melanoma in these rare lesions to ensure appropriate diagnosis and subsequent clinical management as treatment options may be significantly different from those offered for sarcomas.

Key Words: sarcomatoid melanoma, sarcomatoid dedifferentiation, poorly differentiated spindle-cell melanoma

(Am J Dermatopathol 2016;0:1–6)
Case History

- 40 year old male with a 5 cm nodular tumor on the right lateral hip, ?EIC
Diagnosis:

Pigmented DFSP with fibrosarcomatous and myoid differentiation (“Bednar tumor”)
Dermatofibrosarcoma Protuberans
Clinical Presentation

• Young adults (20-40 years)
• Trunk > head & neck and proximal extremities
• Slowly growing plaque >> nodule
• Longstanding history
• Size: ~5cm, often underestimated clinically
Dermatofibrosarcoma Protuberans
Cytogenetics

Reproducible cytogenetic abnormality: t(17;22)
Col1A1 and PDGFB genes

Rarely Col6A3 and PDGFD genes (breast tumors)

Prognosis and Treatment

• High rate of local recurrence
• Low metastatic potential
• Surgery:
  • Wide local excision
  • Modified Mohs surgery at anatomically difficult sites
Dermatofibrosarcoma Protuberans
Variants

- Fibrosarcomatous DFSP
- Pleomorphic DFSP
- DFSP with myoid nodules
- Giant Cell Fibroblastoma
- Pigmented DFSP (“Bednar tumor”)
- Myxoid DFSP
- Atrophic DFSP
Myxoid DFSP
Fibrosarcomatous DFSP