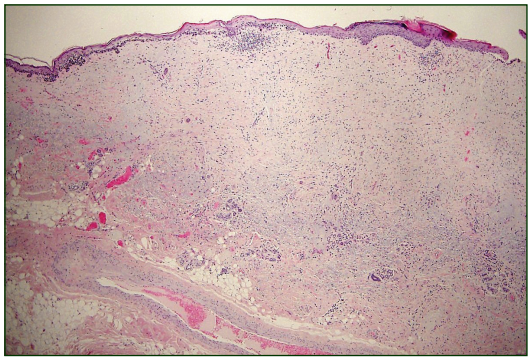
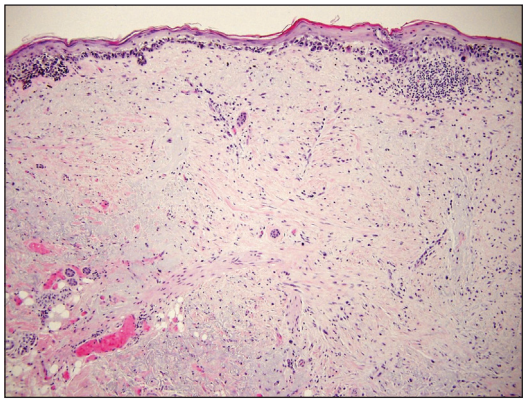


H&E, original magnification ×40.



H&E, original magnification ×100.

The best diagnosis is:

a. atypical fibroxanthoma
b. cutaneous angiosarcoma
c. cutaneous leiomyosarcoma
d. desmoplastic melanoma
e. spindle cell squamous cell carcinoma

PLEASE TURN TO PAGE 313 FOR DERMATOPATHOLOGY DIAGNOSIS DISCUSSION

Christine Schleich, MD; Tammie Ferringer, MD

From the Department of Dermatology, Geisinger Medical Center, Danville, Pennsylvania. Dr. Ferringer also is from the Department of Laboratory Medicine.
The authors report no conflict of interest.
The eTable is available in the Appendix online at www.cutis.com.
Correspondence: Christine Schleich, MD, Department of Dermatology, Geisinger Medical Center, 115 Woodbine Ln, Danville, PA 17822 (caschleich@geisinger.edu).

Desmoplastic Melanoma

Desmoplastic melanoma, an uncommon variant of melanoma, poses a diagnostic challenge to the clinician because the tumors frequently appear as nonspecific flesh-colored or amelanotic plaques or nodules. They are more common in men than in women and are frequently found on the head and neck.[1,2] Their innocuous appearance may lead to a delay in diagnosis and may explain why desmoplastic melanomas often are deeply infiltrative at the time of biopsy. Desmoplastic melanoma arises de novo in approximately one-third of cases.[1] In the remainder of cases, it is seen in conjunction with overlying melanoma in situ, most commonly lentigo maligna melanoma.[1] Histologically, desmoplastic melanomas are characterized by malignant spindle cells within a densely fibrotic stroma (Figure 1). Adjacent lymphoid aggregates and perineural involvement are common features,[2] while pigment and atypical mitoses can be infrequent. Desmoplastic melanoma can be classified as mixed or pure based on the degree of desmoplasia and cellularity. Within mixed desmoplastic melanomas, there are areas that have histologic features of conventional melanomas while others demonstrate more typical desmoplastic characteristics. Pure desmoplastic melanoma has a higher degree of desmoplasia and fewer tumor cells than the mixed type.[1] The pure subtype tends to be less aggressive and is less likely to metastasize to the lymph nodes.[1] In the absence of an in situ component (Figure 2), desmoplastic melanoma may be indistinguishable from other spindle cell tumors on routine hematoxylin and eosin staining; thus, immunohistochemical staining generally is required. The most reliable stains in confirming a diagnosis of desmoplastic melanoma are S100 and SOX10 (SRY-related HMG-box 10)(Figure 3)(eTable).[3]

Atypical fibroxathoma typically presents as a nodule in the head and neck region or other sun-exposed areas in elderly individuals and is more commonly seen in men than in women.[4] Histologically, atypical fibroxanthomas are composed of pleomorphic

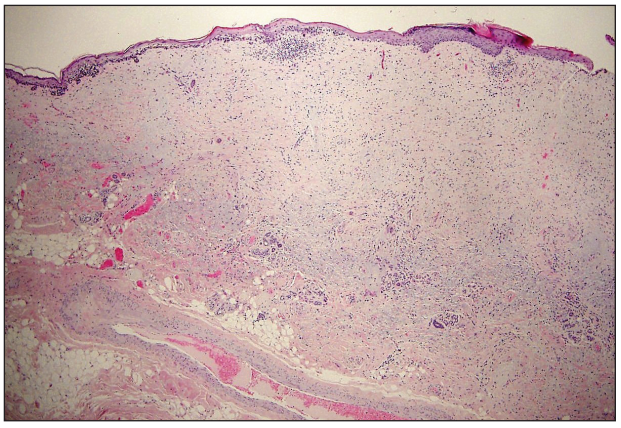


Figure 1. Desmoplastic melanoma with spindle melanocytes in a densely fibrotic stroma (H&E, original magnification ×40).

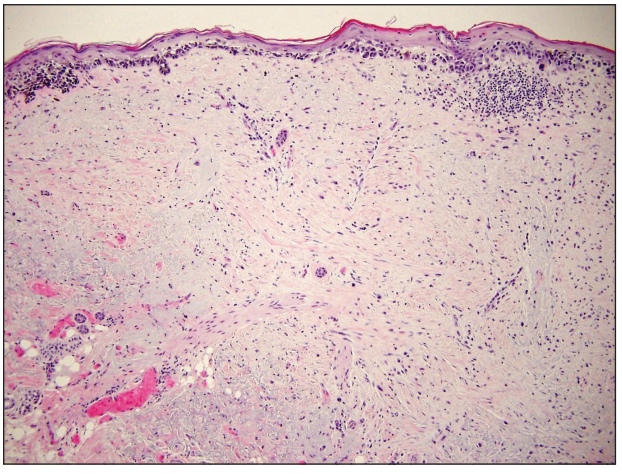


Figure 2. Confluence of atypical melanocytes along the dermoepidermal junction consistent with melanoma in situ overlying desmoplastic melanoma (H&E, original magnification ×100).

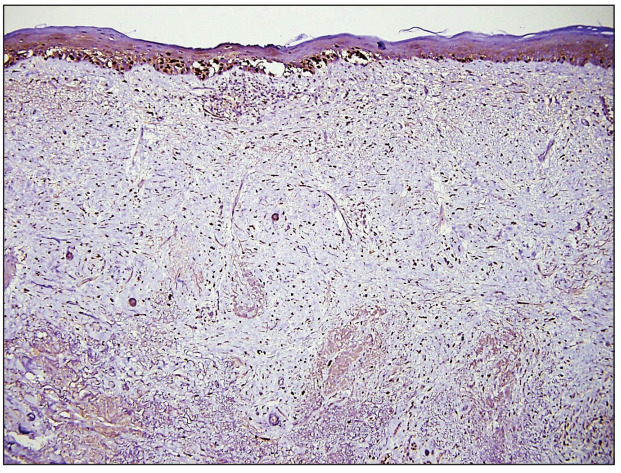


Figure 3. SOX10 (SRY-related HMG-box 10) nuclear expression of spindle melanocytes in the fibrotic dermis and overlying confluence of melanocytes at the dermoepidermal junction in desmoplastic melanoma (original magnification ×100).

spindle, epithelioid, and multinucleated giant cells with numerous and atypical mitoses (Figure 4).[5] Atypical fibroxanthoma is considered a diagnosis of exclusion; therefore, other dermal spindle cell tumors need to be ruled out before diagnosis can be made. Atypical fibroxanthomas generally stain negative for cytokeratin, S100, SOX10, and desmin, but in some cases there is positive focal staining for smooth muscle actin.[4] Multiple immunohistochemical markers, including CD10, have shown reactivity in atypical fibroxanthomas,[4] but none of these markers has a high specificity for this tumor; thus, it remains a diagnosis of exclusion.

Cutaneous angiosarcomas are aggressive tumors associated with a high mortality rate despite appropriate treatment with surgical resection and postoperative radiation treatment. They typically present as ecchymotic macules or nodules on the face or scalp of elderly patients.[6,7] Ionizing radiation and chronic lymphedema are risk factors for cutaneous angiosarcoma.[6] Histologically, well-differentiated cutaneous angiosarcomas are composed of irregular, anastomosing vascular channels that dissect through the dermis (Figure 5).[6,7] Less well-differentiated tumors may contain spindle cells and lack obvious vascular structures; thus immunohistochemistry is essential for making the correct diagnosis in these cases. Cutaneous angiosarcomas typically stain positive for ERG (ETS-related gene) protein, CD31, CD34, and factor VIII.[6,8] Unfortunately these tumors may also occasionally stain with cytokeratin, which may lead to the erroneous diagnosis of a carcinoma.[6]

Cutaneous leiomyosarcoma is a smooth muscle neoplasm that arises from arrector pili muscles, genital smooth muscles, or vascular smooth muscles. It typically presents as a single plaque or nodule on the arms and legs of individuals older than 50 years of age.[9] Cutaneous leiomyosarcomas can be classified as either dermal, in which at least 90% of the tumor is confined to the dermis, or subcutaneous; this distinction is important because the latter type has a higher rate of metastasis and a poorer prognosis.[9] Because of this tumor's smooth muscle derivation, well-differentiated tumors may retain features of typical smooth muscle cells, including cigar-shaped nuclei with adjacent glycogen vacuoles (Figure 6). If fascicle formation is observed, this may be an additional clue to the diagnosis. In poorly differentiated tumors, immunohistochemistry is invaluable.

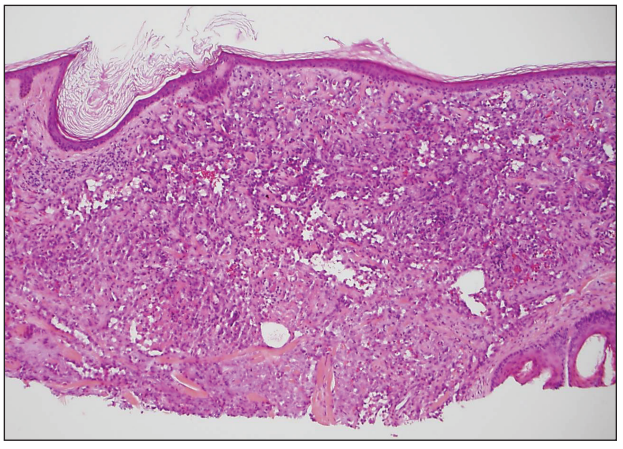


Figure 5. Anastamosing vascular channels dissecting through collagen bundles and consuming the epidermis in cutaneous angiosarcoma (H&E, original magnification ×100).

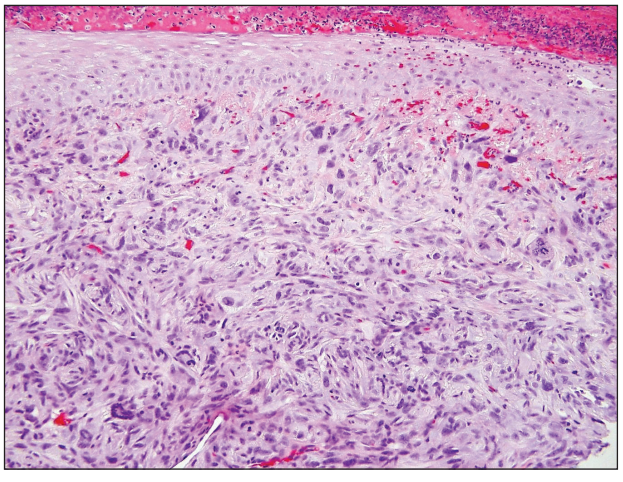


Figure 4. Pleomorphic spindle, epithelioid, and multinucleate giant cells with atypical mitoses filling the dermis in atypical fibroxanthoma (H&E, original magnification ×200).

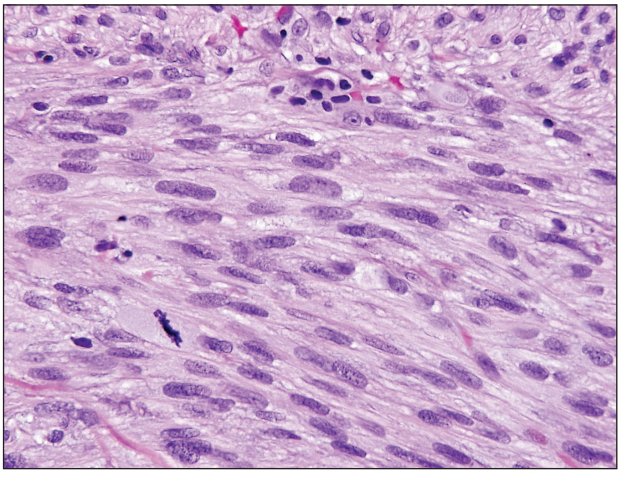


Figure 6. Spindle cells of leiomyosarcoma with cigar-shaped nuclei and adjacent glycogen vacuoles (H&E, original magnification ×600).

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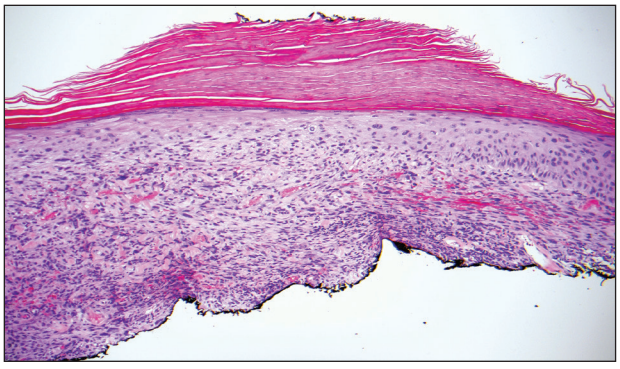

Figure 7. Spindle cell squamous cell carcinoma with overlying epidermal atypia that blends with the underlying dermal spindle cells (H&E, original magnification ×100).

Leiomyosarcoma often stains positive for smooth muscle actin, muscle specific actin, h-caldesmon, desmin, and calponin.[9-11]

Spindle cell squamous cell carcinomas often present as ulcerated nodules on sun-exposed skin or on sites of prior ionizing radiation.[2,12] Like desmoplastic melanoma, spindle cell squamous cell carcinomas are characterized by spindle cells in the dermis. Helpful diagnostic clues may include evidence of squamous differentiation, including keratin pearls or overlying actinic keratosis (Figure 7). However, actinic keratosis is common on sun-damaged skin and cannot be used to definitively confirm this diagnosis. There also may be areas of the tumor with more typical epithelioid cells that are easily identified as squamous cell carcinoma.[2] Spindle cell squamous cell carcinoma stains positive for high–molecular weight cytokeratin antibodies and p63,[2] which can help to differentiate it from the other spindle cell tumors in the differential.

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APPENDIX

Immunohistochemical Markers for Spindle Cell Tumors[a]

Tumor	Cytokeratin	p63	S100	SOX10	Desmin	h-caldesmon	Calponin	SMA	CD10	CD31	ERG
Desmoplastic melanoma	−	−	++	++	−	NA	−	−	−/+	−	NA
Atypical fibroxanthoma	−	−/+	−	−	−	−	−/+	−/+	+	−/+	−
Cutaneous angiosarcoma	−/+	−	−	NA	−	−	NA	−/+	−/+	++	++
Cutaneous leiomyosarcoma	−/+	−/+	−/+	NA	+	+	+	++	−/+	−	−
Spindle cell SCC	+	+	−	−	−	NA	−	−	−/+	−	NA

Abbreviations: SOX10, SRY-related HMG-box 10; SMA, smooth muscle actin; ERG, ETS-related gene protein; NA, not available; SCC, squamous cell carcinoma.

[a]Sensitivity graded as: ++, positive in >90% of cases; +, positive in >70% of cases; +/−, positive in >50% of cases; −/+, positive in <50% of cases; −, positive in <5% of cases.