Case Report

Pleomorphic Dermal Sarcoma: A Clinical and Histopathologic Emulator of Atypical Fibroxanthoma, but Different Biologic Behavior

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Abstract

Description

Pleomorphic dermal sarcoma (PDS) can clinically and histopathologically mimic atypical fibroxanthoma (AFX). However, it has a more aggressive clinical course with a higher recurrence rate and metastatic potential. This case presentation aims to report a rapidly-growing, exophytic, 4 cm tumor following a non-diagnostic shave biopsy 2 months prior and to highlight distinctive features between PDS and AFX needed to make the correct diagnosis. Like AFX, PDS occurs on the sun-damaged skin of the elderly, usually on the head and neck. Also, like AFX, PDS histopathologically consists of sheets or fascicles of epithelioid and/or spindle-shaped cells, often with multinucleation, pleomorphism, and numerous mitotic figures. Immunohistochemistry cannot distinguish PDS from AFX but is used to exclude other malignancies. PDS can be distinguished from AFX by size (PDS is usually >2.0 cm) and by the presence of more aggressive histopathologic features, such as subcutaneous involvement, perineural and/or lymphovascular invasion, and necrosis. PDS is a rare entity not well documented in the literature with confusing, misleading, and changing nomenclature. PDS is a diagnosis of exclusion made after complete excision of the tumor with the aid of histopathology and immunohistochemistry.

Keywords

pleomorphic dermal sarcoma; PDS; undifferentiated pleomorphic sarcoma; UPS; atypical fibroxanthoma; AFX; malignant fibrous histiocytoma; MFH; diagnosis of exclusion; differential diagnosis; neoplasms

Introduction

Atypical fibroxanthoma (AFX) and pleomorphic dermal sarcoma (PDS) can be indistinguishable by clinical appearance and histopathologic findings on the initial biopsy.[1] Distinguishing between the two is essential, as the prognoses of these tumors are vastly different. AFX follows a benign course, typically recurring only after incomplete excision, and rarely metastasizes. PDS is more aggressive and has a higher recurrence rate and metastatic potential. AFX presents as a rapidly-growing, solitary papule or nodule on sun-damaged, actinic skin of the elderly, usually on the head and neck region. PDS can have a similar presentation and should be considered with larger tumors, particularly when greater than 2.0 cm.[2-4] Similar tumors arising from the deep soft tissue and extending into the skin should be designated as undifferentiated pleomorphic sarcoma (UPS). These are high-grade soft tissue tumors with high rates of recurrence and metastases.[5] PDS has also been designated "UPS of the skin," but the use of this terminology should be avoided as it may cause confusion among healthcare providers.[2,5]

On biopsy, AFX and PDS (as well as UPS) are pleomorphic tumors. They are diagnoses of exclusion, requiring broad lineage-specific immunohistochemical analysis to exclude other

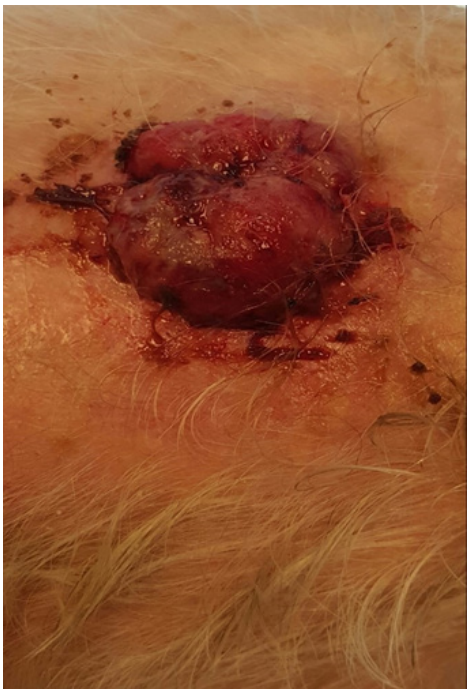

Figure 1. A 4.0 x 2.5 cm ulcerated, friable, exophytic mass presented on the left mid-frontal scalp of an over 89-year-old Caucasian male.

poorly differentiated tumors such as squamous cell cancer and melanoma, among others. Distinguishing these entities requires complete excision to evaluate for aggressive features, specifically the tumor's extent of invasion, with AFX restricted to the dermis.[6,7] We present this case to increase awareness of this rare sarcoma, highlight its characteristic histopathologic and immunophenotypic features, and emphasize the importance of complete excision of tumors initially classified as AFX to prevent mismanagement of an aggressive and potentially fatal tumor.

Case Presentation

An over 89-year-old Caucasian man with a history of several non-melanoma skin cancers presented with a 4.0 x 2.5 cm ulcerated, friable, exophytic mass on the left mid-frontal scalp of 2 months duration (**Figure 1**).

The patient had previously presented 2 months earlier with a non-healing scalp lesion. The lesion was a 0.9 cm ulcerated, erythematous papule at that time. Histopathology of a shave biopsy was non-diagnostic and demonstrated marked parakeratosis, fibrosing granulation tissue in the upper dermis, with a heavy inflammatory infiltrate.

A repeat biopsy of the exophytic mass was performed for diagnostic and de-bulking purposes. The histopathology of the re-biopsy demonstrated an ulcerated tumor filling the dermis. The tumor cells were pleomorphic, spindled, and arranged in vague fascicles (**Figure 2**). The cytology was markedly atypical, with large irregular nuclei, prominent nucleoli, and numerous mitoses, including atypical forms (**Figure 3**). An immunohistochemical analysis was performed. The tumor cells were diffusely positive for CD10 and weakly positive for CD68. Cytokeratin AE1/AE3, cytokeratin 5, p63, S-100, MART-1, desmin, smooth muscle myosin, CD31, and CD34 were all negative. While these findings were consistent with AFX, complete excision was recommended to exclude a more aggressive process.

The patient subsequently underwent wide local excision with 1-centimeter margins. The specimen showed atypical spindled cells extending deep into the subcutaneous tissue (**Figure 4**). Due to the depth of invasion and the subcutaneous tissue involvement, the lesion was diagnosed as PDS (previously diagnosed as UPS of the skin). The margins were free of tumor. The patient was referred to oncology for further evaluation and consideration of adjuvant therapy. The patient and family declined the oncol-

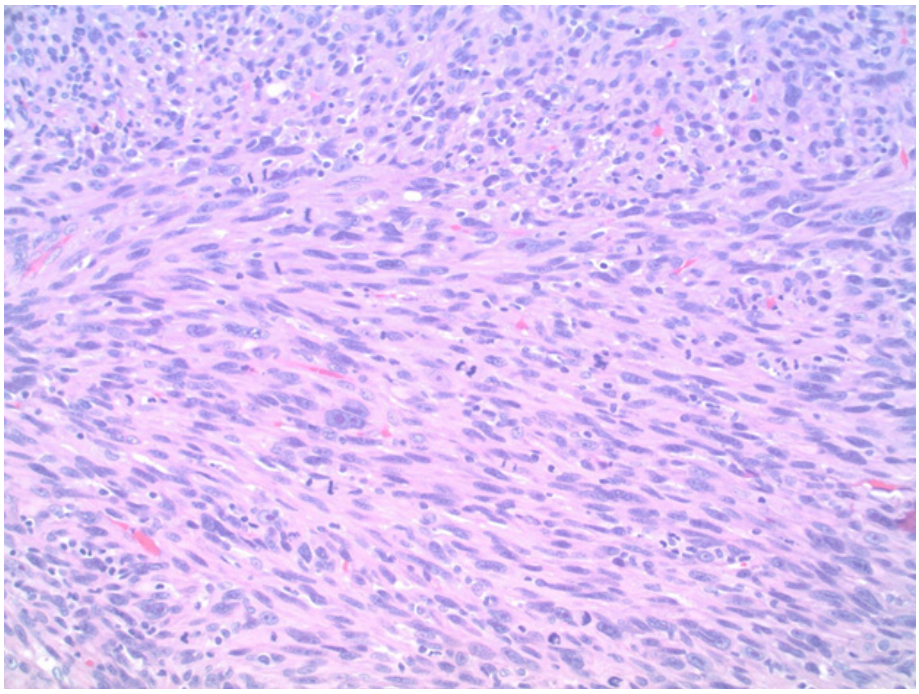

Figure 2. Histopathology hematoxylin and eosin stain of re-biopsy showed pleomorphic spindled cells arranged in fascicles within the dermis.

ogy referral. At 4 months post-excision, there was no evidence of tumor recurrence.

Discussion

Clinically, AFX can be indistinguishable from PDS. However, they are vastly different. These two diseases differ in clinical course and prognosis. A correct diagnosis is crucial to an optimal outcome. Both present as rapidly growing solitary nodules, usually occurring on the head and neck of sun-damaged skin of the elderly that frequently ulcerate, causing bleeding.[1]

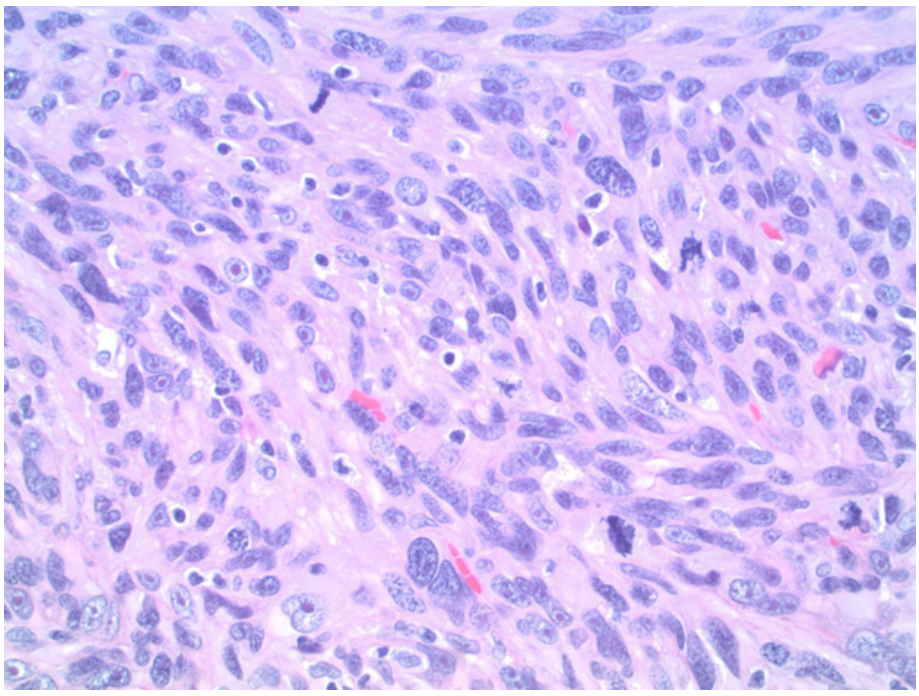

Figure 3. A close-up view of hematoxylin and eosin stain showed atypical cytology, with large irregular nuclei, prominent nucleoli, and numerous mitoses.

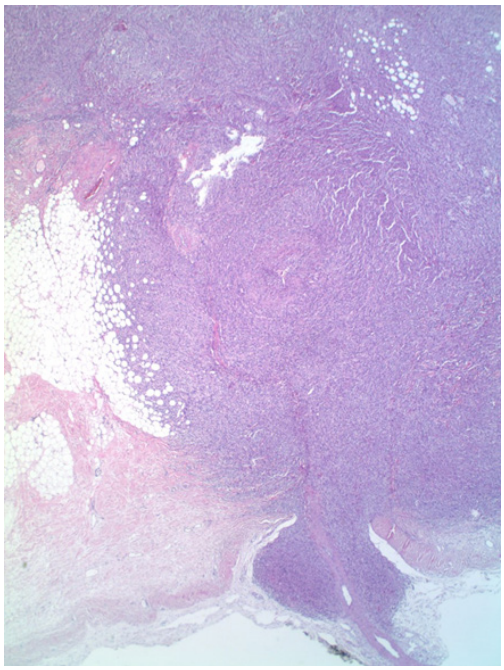

Figure 4. Specimen of wide local excision specimen showed atypical spindled cells extending deep into the subcutaneous tissue.

Ultraviolet (UV) exposure and previous radiation treatment are considered major risk factors with these tumors since they have a predilection for occurring on sun-exposed skin. AFX is typically less than 2.0 cm in diameter, located superficially within the dermis, and neither involves the subcutis nor invades deeper structures such as the fascia or muscle.[2-4] AFX follows a benign course. The diagnosis of AFX needs to be strictly defined so that it is not grouped with other pleomorphic tumors of the skin or deeply invasive sarcomas known to have metastatic potential.[5]

The nomenclature of these entities has evolved. Terms such as AFX, PDS, superficial UPS, UPS of the skin, UPS, and malignant fibrous histiocytomas (MFH) have all been used to describe this family of tumors, which share histopathologic and immunohistochemical features. With advancements in immunohistochemistry, many lesions previously called MFH have now been reclassified into lineage-specific sarcomas, such as liposarcoma, leiomyosarcoma, rhabdomyosarcoma, malignant peripheral nerve sheath tumor, extraskeletal osteosarcoma, and sarcomatoid carcinoma. Malignant fibrous histiocytoma is no longer considered a distinct entity.[5]

Histologically, AFX and PDS (and UPS) consist of spindle-shaped cells arranged in sheets or a fascicular pattern and can exhibit multinucleation, pleomorphism, and mitotic figures.[5] Immunohistochemically, these tumors often have a strong expression for CD10, but this marker lacks specificity. They are negative for other lineage-specific markers, such as cytokeratins, S-100, CD31/CD34, and desmin/myosin, allowing distinction from spindled squamous cell carcinomas, melanoma, angiosarcoma, and leiomyosarcoma, respectively.[6,7]

Tumors with AFX-like histopathology on biopsy but are clinically greater than 2.0 cm centimeters in diameter should raise concern for a more aggressive tumor. If the tumors have a subcutaneous invasion, perineural invasion, lymphovascular invasion, and/or necrosis, they are best classified as PDS. UPS is a better designation if they arise from the deep soft tissue. Our case illustrates the importance of recognizing this distinction, as the lesion was greater than 2 cm, showed subcutaneous involvement along with necrosis, and was negative for lineage-specific immunohistochemical stains. The clinical course of beginning as a superficial papule suggests an origin in the skin rather than deep soft tissues. PDS carries a more aggressive course, risk of recurrence, and metastatic potential compared to AFX.[8]

Arriving at the diagnosis of AFX or PDS can be challenging and is one of exclusion. Both diagnoses require extensive immunohistochemical panels to exclude other common pleomorphic tumors in the skin, such as melanoma, squamous cell carcinoma, angiosarcoma, and leiomyosarcoma.[7,9,10] At a minimum, negative staining for S-100/SOX10, cytokeratin, CD31/CD34, and myosin/desmin should be confirmed to exclude other diseases in the differential diagnosis.[7] The separation of AFX and PDS can only be made with larger tumors and/or when significant subcutaneous tissue is available for analysis on complete excision, showing aggressive features such as invasion into the subcutaneous tissue, tumor necrosis, and/or perineural or lymphovascular invasion.[8] While it is known that AFX is a rare tumor, the diagnosis of PDS is even rarer, and its characteristics are less documented in the literature.[11,12]

The distinction between AFX and PDS is vital since they have similar clinical, histologic, and immunohistochemical presentations, but their behavior is vastly different. AFX follows a more benign course with a reported infrequent local recurrence rate, shown to be less than 5%, and is most commonly associated with an incomplete removal.[9,10,13] Evidence suggests an even lower risk of recurrence when AFX is treated with Mohs micrographic surgery.[14] Most of the reported cases of AFX with metastasis in the literature were before the availability of immunohistochemistry. These were likely other pleomorphic malignancies and probably represent misdiagnoses.[6]

In contrast, PDS behaves more aggressively and recurs at a greater rate, along with greater metastatic potential.[8] The local recurrence rate of PDS has been reported as 28%, and the risk for metastasis is 10%.[15] Despite the morphologic features of a high-grade sarcoma, the overall disease course of PDS is more in line with that of low-grade malignancy. Disease-related mortality is rare, but long-term clinical follow-up is difficult to obtain due to the advanced age at presentation and other comorbidities.[8]

Tumors designated as PDS, UPS of the skin, superficial UPS, and a superficial variant of MFH all likely represent the same entity as all have similar clinical features with histopathologic characteristics of morphologically high-grade tumors with a lack of lineage-specific differentiation.[16,17] PDS is the preferred term as it causes less confusion. More importantly, there is a distinction among PDS, AFX, UPS, and MFH due to differences in clinical course and prognosis.[5,8,13,18]

Conclusion

There is significant clinical and histopathologic overlap between AFX and PDS. However, if present, the tumor's clinical size and aggressive histopathological features can help with distinction. Tumors greater than 2.0 cm and/or tumors with histopathologic features, such as invasion of subcutaneous tissue, tumor necrosis, and perineural or lymphovascular invasion, are best classified as PDS. These features are consistent with its more aggressive course, including recurrence and metastatic potential.

In our case, the lesion was a cutaneous, rapidly-growing, solitary tumor that was greater than 2 cm and was on the sun-damaged scalp of an elderly male. The immunohistochemical profile of the tumor showed a high-grade pleomorphic sarcoma without specific lineage differentiation. On excision, the subcutaneous tissue was involved along with tumor necrosis, leading to a diagnosis of PDS. The correct diagnosis ultimately required excision, histopathology, and immunohistochemistry.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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References

1. Fibrous and fibrohistiocytic proliferations of the skin and tendons, atypical fibroxanthoma. In: Bolognia JL, Jorizzo JL and Schaeffer JV, eds. *Dermatology*. 3rd ed. Elsevier; 2012:1973.
2. Elder DE, Massi D, Scolyer RA, Willemze R, eds. *WHO Classification of Skin Tumours*. World Health Organization; 2018.
3. Winchester D, Lehman J, Tello T, et al. Undifferentiated pleomorphic sarcoma: factors predictive of adverse outcomes. *J Am Acad Dermatol*. 2018;79(5):853-859.
4. Iglesias-Pena N, Martínez-Campayo N, López-Solache L. Relation between atypical fibroxanthoma and pleomorphic dermal sarcoma: histopathologic features and review of the literature. Relación entre fibroxantoma atípico y sarcoma pleomórfico dérmico: histopatología de ambos y revisión de la literatura. *Actas Dermosifiliogr (Engl Ed)*. 2021;112(5):392-405. doi:10.1016/j.ad.2020.11.018
5. Undifferentiated pleomorphic sarcoma. In: Goldblum JR, Folpe AL, Weiss SW. *Enzinger and Weiss's Soft Tissue Tumors*. 6th ed. Elsevier; 2014:421-442.
6. Connective tissue tumors, atypical fibroxanthoma, malignant fibrous histiocytoma. In: Calonje E, Brenn T, Lazar A, McKee PH. *McKee's Pathology of the Skin*. 4th ed. Elsevier; 2012:1658-1662.
7. Luzar B, Calonje E. Morphological and immunohistochemical characteristics of atypical fibroxanthoma with a special emphasis on potential diagnostic pitfalls: a review. *J Cutan Pathol*. 2010;37(3):301-309. doi:10.1111/j.1600-0560.2009.01425.x
8. Miller K, Goodlad JR, Brenn T. Pleomorphic dermal sarcoma: adverse histologic features predict aggressive behavior and allow distinction from atypical fibroxanthoma. *Am J Surg Pathol*. 2012;36(9):1317-1326. doi:10.1097/PAS.0b013e31825359e1
9. Beer TW, Drury P, Heenan PJ. Atypical fibroxanthoma: a histological and immunohistochemical review of 171 cases. *Am J Dermatopathol*. 2010;32(6):533-540. doi:10.1097/DAD.0b013e3181c80b97
10. Mirza B, Weedon D. Atypical fibroxanthoma: a clinicopathological study of 89 cases. *Australas J Dermatol*. 2005;46(4):235-238. doi:10.1111/j.1440-0960.2005.00190.x
11. Anderson HL, Joseph AK. A pilot feasibility study of a rare skin tumor database. *Dermatol Surg*. 2007;33(6):693-696. doi:10.1111/j.1524-4725.2007.33145.x
12. Withers AH, Brougham ND, Barber RM, Tan ST. Atypical fibroxanthoma and malignant fibrous histiocytoma. *J Plast Reconstr Aesthet Surg*. 2011;64(11):e273-e278. doi:10.1016/j.bjps.2011.05.004
13. Fretzin DF, Helwig EB. Atypical fibroxanthoma of the skin. A clinicopathologic study of 140 cases. *Cancer*. 1973;31(6):1541-1552. doi:10.1002/1097-0142(197306)31:6<1541::aid-cncr2820310635>3.0.co;2-6
14. Ang GC, Roenigk RK, Otley CC, Kim Phillips P, Weaver AL. More than 2 decades of treating atypical fibroxanthoma at mayo clinic: what have we learned from 91 patients?. *Dermatol Surg*. 2009;35(5):765-772. doi:10.1111/j.1524-4725.2009.01126.x
15. Davidson JS, Demsey D. Atypical fibroxanthoma: clinicopathologic determinants for recurrence and implications for surgical management. *J Surg Oncol*. 2012;105(6):559-562. doi:10.1002/jso.22128
16. McCalmont TH. Correction and clarification regarding AFX and pleomorphic dermal sarcoma. *J Cutan Pathol*. 2012;39(1):8. doi:10.1111/j.1600-0560.2011.01851.x
17. Fletcher CD. The evolving classification of soft tissue tumours - an update based on the new 2013 WHO classification. *Histopathology*. 2014;64(1):2-11. doi:10.1111/his.12267
18. Mentzel T. Sarcomas of the skin in the elderly. *Clin Dermatol*. 2011;29(1):80-90. doi:10.1016/j.clindermatol.2010.07.011