

# Atypical Fibroxanthoma: A Case Report and Literature Review

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## Abstract

*Atypical fibroxanthoma (AFX) is a rare, rapidly growing mesenchymal neoplasm that often presents on sun-exposed head and neck regions of older individuals. The diagnosis relies on knowledge of its clinical and histological features combined with immunohistochemistry markers used primarily to exclude other cutaneous neoplasms that may share a similar clinical presentation. Current treatment guidelines recommend wide local excision or Mohs micrographic surgery to prevent local recurrence and, on rare instances, metastasis of AFX, combined with long-term clinical monitoring. We report the case of an 88-year-old male presenting with a rapidly growing atypical fibroxanthoma and discuss diagnosis and treatment of this rare cutaneous neoplasm.*

## Introduction

Atypical fibroxanthoma (AFX) is a rare, rapidly growing, mesenchymal neoplasm that comprises 0.2% of skin tumors.<sup>1,2</sup> AFX was first described in 1963 by Helwig et al. as a low-grade dermal tumor consisting of atypical spindle cells with an uncertain etiology.<sup>3</sup> Since then, research has supported that AFX likely arises from a fibroblast or myofibroblast-like cell. The most widely agreed upon predisposing factor for development of AFX is ultraviolet (UV) radiation exposure.<sup>1,2,4,5</sup> Additional risk factors include a history of radiation exposure, previous burn or trauma to the area, immune suppression, and a history of xeroderma pigmentosa.<sup>2,4-6</sup> In a recent review, Koch et al. determined that the majority of cases occur on sun-exposed head and neck regions in males in their 5<sup>th</sup> to 7<sup>th</sup> decade of life, with a mean age of 75.8.<sup>1</sup> Fewer cases occurred on non-sun-exposed regions, such as the trunk and limbs, of a slightly younger population. Other reports have indicated that AFX occurs in patients ranging from 3 to 115 years old.<sup>1,7</sup>

Clinically, an atypical fibroxanthoma (AFX) manifests as an asymptomatic, solitary, rapidly growing, exophytic papule or nodule.<sup>4,5</sup> The overlying skin may be smooth and intact with a yellow hue, or it may ulcerate and bleed. AFX is rarely pigmented.<sup>2</sup> Typically, the diameter of the nodule is

less than 2 cm, but can range in size from 0.3 cm to 10 cm. Due to its nonspecific clinical appearance, diagnosis of AFX is challenging. Other pathologies to consider based on physical examination include squamous cell carcinoma, basal cell carcinoma, pyogenic granuloma, malignant melanoma, adnexal tumor, cutaneous soft tissue sarcoma, and Merkel cell carcinoma.<sup>2,5</sup> Therefore, biopsy is imperative to achieve the correct diagnosis.

AFX was once considered benign secondary to its excellent prognosis. However, reports of metastatic AFX resulting in death have challenged this claim.<sup>1,2</sup> Herein, we report the case of an 88-year-old male who presented with a rapidly growing atypical fibroxanthoma and provide a discussion regarding diagnosis and treatment of this rare cutaneous neoplasm.

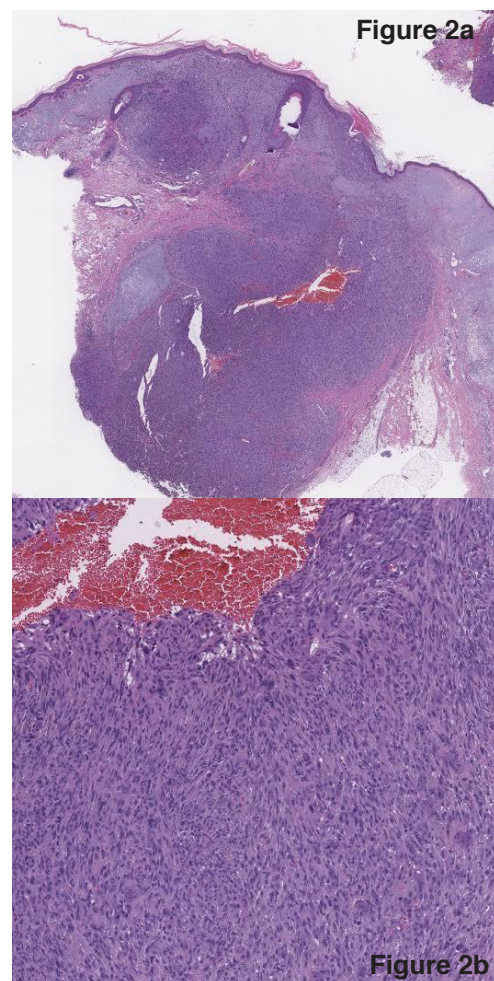
## Case Report

An 88-year-old Caucasian male presented to our dermatology clinic for evaluation of a rapidly enlarging solid cutaneous tumor present for approximately six months on his posterior neck. He denied associated symptoms of pain, pruritus, tenderness, or bleeding. His past medical history was significant for basal cell carcinoma, squamous cell carcinoma, and prostate cancer. Family history was noncontributory.

On clinical examination, his left posterior neck had a solitary, fixed and firm, nontender, red to slightly blue, indurated nodule measuring 1.0 cm x 0.8 cm (**Figure 1**). Significant solar elastosis of surrounding skin was observed. A saucerization biopsy was performed to remove the bulk of the tumor, which was sent to a dermatopathology laboratory for tissue processing. The differential diagnosis included basal cell carcinoma, squamous cell carcinoma, metastatic prostate carcinoma, atypical fibroxanthoma, cutaneous soft tissue



Figure 1. AFX on left posterior neck with background of solar elastosis.



Figures 2a (1x), 2b (5x). H&E stain demonstrating atypical spindle epithelial cells with mitosis and multinucleated giant cells.



sarcoma, leiomyosarcoma, amelanotic malignant melanoma, and dermatofibrosarcoma protuberans. The dermatopathology report described sheet-like and fascicular proliferation of atypical spindled cells with admixed multinucleate giant cells using hematoxylin and eosin (H&E) staining (Figures 2a, 2b). Atypical mitotic figures were readily observed along with focal intralesional hemorrhage with siderophage accumulation. Immunohistochemistry demonstrated strong positivity of spindle cells for CD10 and some associated smooth muscle actin (SMA) positivity (Figures 3, 4). Immunohistochemistry was negative for S-100 protein, SOX10, cytokeratin 5/6, high molecular weight keratin and desmin. The surgical margins were positive.

Our patient was referred for Mohs micrographic surgery, which required two stages for tumor clearance. The resulting defect measured 4.5 cm x 4.0 cm and was reconstructed with a complex linear closure. The patient is currently followed in our dermatology clinic monitoring for AFX recurrence and metastasis.

### Discussion

Atypical fibroxanthoma (AFX) is typically a diagnosis of exclusion that requires histopathologic and immunohistochemical analysis to distinguish it from tumors with similar clinical and microscopic appearances. Histopathologically, AFX appears extremely abnormal, with a dermal proliferation of haphazardly arranged spindle cells, multinucleated giant cells, or epithelioid cells that demonstrate pleomorphism with frequent mitotic figures, hyperchromatic nuclei, and intracytoplasmic lipidization.<sup>2,4</sup> There are several AFX variants based on microscopic morphology. These include spindle cell, desmoplastic, granular, angiomatoid, hemosiderin pigmented, osteoid, clear cell, chondroid, keloidal, and myxoid.<sup>4,5,8</sup>

Due to a lack of distinguishing morphological features, immunohistochemical analysis is required to differentiate AFX from spindle cell and squamous cell carcinoma, malignant melanoma (specifically the desmoplastic variant), leiomyosarcoma, and undifferentiated pleomorphic sarcoma (formerly known as myxofibrosarcoma or malignant fibrous histiocytoma).<sup>5</sup> There is no immunohistochemical stain specific for AFX; however, this tumor should stain positive for vimentin, CD10, CD68, and smooth muscle actin. Additionally, AFX should stain negative for CAM5.2, CD34, Melan-A, S100, HMB-45, cytokeratin AE1/AE3, and cytokeratin 5/6. If a tumor stains positive for cytokeratins,

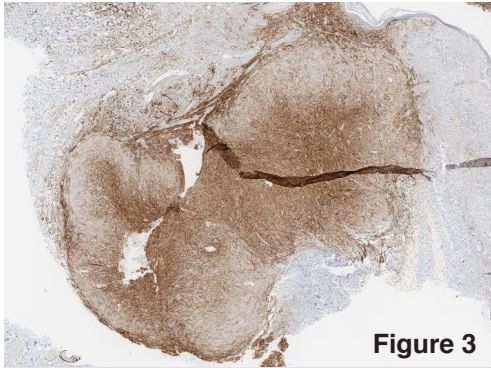


Figure 3 (1x). Positive CD10 showing significant brown staining of AFX on left posterior neck.

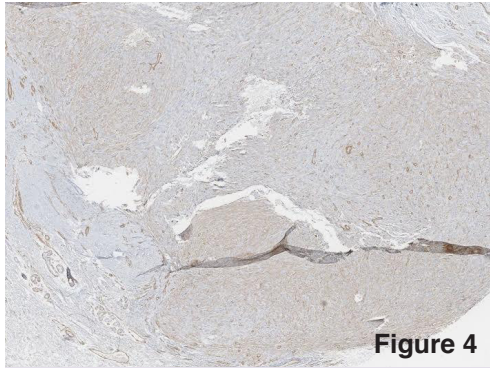


Figure 4 (5x). Positive SMA showing light brown staining of AFX on left posterior neck.

it helps differentiate a spindle cell SCC from AFX. Furthermore, if S100 and SOX-10 stains positive, this frequently distinguishes desmoplastic melanoma from AFX. Finally, a staining pattern positive for desmin, smooth muscle actin, and h-Caldesmon discerns a leiomyosarcoma from AFX (Table 1).<sup>1,4,5</sup>

Although the goal of immunohistochemical analysis is to distinguish AFX from other tumors in its histopathologic differential diagnosis, clinical correlation is required because of the potential for stain cross-reactivity and/or aberrant staining among neoplasms. Moreover, undifferentiated pleomorphic sarcoma (UPS) is argued to be histopathologically and immunohistochemically indistinguishable from AFX.<sup>1,4</sup> In fact, some argue that AFX is a superficial type of UPS. However, a study by Lazova et al. suggested LN-2 stain may be specific to UPS (Table 1).<sup>9</sup> It is also proposed that identification of H-ras, K-ras, and N-ras mutations by gene analyses is diagnostic of UPS since these mutations are absent in AFX.<sup>4,8</sup> Additionally, analyzing the deep component of a biopsy may be helpful in differentiating AFX from UPS, as evidence of subcutaneous fat invasion, perineural or vascular invasion, or necrosis favors the more aggressive UPS neoplasm.<sup>2</sup> Distinguishing between AFX and UPS is critical because the latter has significantly higher rates of recurrence and metastasis.<sup>4</sup> Still, there have been limited cases of metastatic AFX with aggressive characteristics indicative of a poorer prognosis.<sup>2</sup>

Other primary tumor characteristics of an AFX that may indicate a more aggressive course include increased tumor size, depth, ulceration, and necrosis.<sup>10</sup> Patient status is also important when

predicting the clinical course of AFX. Patients with a history of radiation therapy or those who are immunocompromised have a higher risk for AFX recurrence or metastasis.<sup>10</sup> Previously reported locations for AFX metastases include parotid gland (most common), subcutaneous fat, lymph nodes, lungs, and abdomen.<sup>6,10</sup> Because AFX has the potential to recur and metastasize, initial treatment should focus on complete excision with clear margins.

### Treatment

Due to the rarity of AFX, there are no standardized treatment recommendations. Previously reported treatments include wide local excision, Mohs micrographic surgery, modified Mohs micrographic surgery (slow Mohs), radiation therapy, cryotherapy, and electrocautery.<sup>2,6</sup> Since the majority of cases of AFX occur on the head and neck, tissue conservation is a priority.

Mohs micrographic surgery is recommended because it is an efficient treatment modality to spare tissue and obtain tumor-free margins. Most treatment studies focusing on wide local excision or Mohs have shown recurrence rates ranging from 0% to 16%. Furthermore, most of the recurrences occurred within one to two years post-surgery.<sup>11-15</sup> For example, Davis et al. (n=44) showed a 16% recurrence and 0% recurrence in AFX cases treated by wide local excision or Mohs surgery, respectively. The patients treated by wide local excision were followed for an average of 73.6 months, and the Mohs patients were followed for an average of 29.6 months.<sup>11</sup> Huether et al. (n=33) showed patients with AFX treated by Mohs surgery had a 6.9% recurrence rate over an average follow-up of 3.3 years.<sup>16</sup> Finally, Seavolt and McCall treated 13 AFX patients with Mohs surgery and reported

Table 1. Immunohistochemical staining patterns for AFX vs. tumors in histopathologic differential diagnosis

Atypical Fibroxanthoma		Spindle/Squamous Cell Carcinoma	Melanoma	Leiomyosarcoma	Undifferentiated Pleomorphic Sarcoma
Positive	Negative	Positive	Positive	Positive	Positive
Vimentin	Cytokeratins	Cytokeratins	S100	Desmin	CD74
CD68	P63	P63	Melan-A/Mart1	Actin	CD10
CD10	S100		HMB-45	H-Caldesmon	CD99
Procollagen 1	Desmin				MIB-1
CD1A	HMB-45				LN-2 (CD74)
Fascin	Melan-A/Mart1				
A1At	EMA				
CD99	CD34				
	CD31				
	NGFR				
	CD15				
	CD74				

no recurrences; however, the follow-up period was noted to be short.<sup>17</sup>

Radiation or chemotherapy is recommended once an AFX has recurred or metastasized.<sup>2,8</sup> There are rare cases where AFX recurrences or metastases resulted in death. A recent review by Koch et al. showed a 0.7% mortality rate in 1,488 patients with metastatic AFX.<sup>1</sup> Since the literature supports a risk of recurrence or metastasis, and subsequent death from an AFX, regular follow-up is highly encouraged for five years after initial treatment.<sup>6</sup> Although Mohs micrographic surgery is favored for primary AFX, physicians must use their clinical judgment to determine treatment based on patient status, comorbidities, and life expectancy.

## Conclusion

Atypical fibroxanthoma is currently considered to have an intermediate malignant potential requiring timely diagnosis and treatment. It is a rare neoplasm that commands a multi-step diagnostic process including a biopsy with histopathologic analysis, immunohistochemical staining, and potentially genetic analysis. Once identified, Mohs micrographic surgery is supported as the best treatment modality for obtaining tumor-free margins and conserving healthy tissue. If treated appropriately, AFX has an excellent prognosis. However, there is a low risk of recurrence, metastasis, and death from a primary AFX. Therefore, regular long-term monitoring for AFX recurrence and metastasis is required.

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