Introduction

Atypical fibroxanthoma (AFX) is a rare skin condition, and both its cause and its classification are still debated. AFX is currently known as a rare cutaneous fibrohistiocytic tumor, but the term AFX was first used by Helwig in 1961 to describe a dermal tumor of atypical spindle cells. Clinically, two variants of AFX have been described. The more common clinical variant presents on sun-exposed areas, such as the head and neck, in older patients (median age 69). The less common clinical variant presents in non-sun-exposed areas in younger patients (median age 39), as it did in our patient. Histologically, this tumor had to be differentiated from other malignant skin cancers. In addition, it has been argued that this tumor may be a superficial undifferentiated pleomorphic sarcoma (UPS). This case report brings awareness to this rare skin cancer, delineates its two clinical subsets and discusses its controversial histological origins.

Case Report

A 38-year-old man presented to the clinic with a 7 mm, erythematous papule with rolled borders and a central ulcer on the right posterior thigh (Figures 1 and 2). The lesion was originally observed by the patient approximately two months prior to his office visit. The patient reported a change in both the size and color of the lesion, as well as episodes of bleeding. There were no associated symptoms of pain or pruritus. Medical history was unremarkable. A shave biopsy was performed to rule out a keratoacanthoma versus squamous cell carcinoma versus pyogenic granuloma.

Pathology revealed an ulcerated, atypical spindle cell proliferation (Figures 3a, 3b). The atypical dermal spindle cells were CD68 (Figure 4) and CD163 positive (Figure 5) but negative for melan-A, S100, factor 13A, and CD34. Smooth muscle actin (SMA) stained positively around blood vessels. The immunohistochemical findings were consistent with fibro-histiocytic differentiation and most consistent with AFX. Treatment as a low-grade sarcoma was recommended. A complete excision was performed, and the patient has experienced no recurrence of the lesion.

Discussion

AFX is a rare cutaneous fibrohistiocytic tumor of low to intermediate metastatic potential. Due to its rarity, the incidence of AFX is unknown. AFX mainly occurs on sun-exposed skin in elderly white males during the eighth decade.
of life. However, there is a subset of younger patients with AFX on non-sun-exposed areas, such as the trunk and extremities, during the fourth decade of life. AFX usually presents as a rapidly growing lesion on sun-damaged skin such as the nose, cheeks, ears, neck or scalp. The median time between onset and biopsy or excision is four months. The lesion is usually a red or pink, solitary, asymptomatic papule or dome-shaped nodule that is less than 2 cm in diameter and may be eroded or ulcerated. The non-sun-exposed clinical variant tends to be slightly larger and has a longer duration from onset to biopsy or excision. Clinically, an AFX lesion may resemble SCC, basal cell carcinoma (BCC), or necrotic pyogenic granuloma. Since AFX has nonspecific clinical features, diagnosis requires a biopsy. A personal history of skin cancers like BCC or SCC is common in patients with AFX.

The histopathology of AFX generally demonstrates a dermal circumscribed hyperecellular tumor that may extend deep into the reticular dermis and consists of a mixture of highly pleomorphic spindle cells, epithelioid cells, and multinucleated giant cells. The proportion of cell types in a lesion varies, and the neoplastic cells display a pronounced atypia proportion of cell types in a lesion varies, and the neoplastic cells display a pronounced atypia. The overlying epidermis of the lesions on the head and neck are usually atrophic or ulcerated, whereas lesions on the trunk and extremities frequently extend into the subcutis. The overlying epidermis and hyperkeratosis and parakeratosis is common. In contrast, the epidermis of lesions of the trunk and extremities is often normal or acanthotic.

Currently, no single immunohistochemical marker is specific for AFX. Therefore, multiple markers must be used, including those for other similar histologic diseases. Specifically, immunohistochemistry helps differentiate AFX from spindle cell SCC, desmoplastic melanoma, leiomyosarcoma, and undifferentiated pleomorphic sarcoma (UPS, formerly known as pleomorphic malignant fibrous histiocytoma [MFH]). UPS is a soft tissue sarcoma that occurs primarily in deep soft tissue. Since the histology of AFX and UPS is identical, some consider AFX to be a less aggressive, superficial variant of UPS.

Histologic differences exist between the two clinical variants (head and neck/sun-exposed areas versus trunk and extremities/non-sun-exposed areas) (Table 1). Lesions of the head and neck (the more common variant’s location of presentation) tend to be relatively smaller and better demarcated than lesions on the trunk and extremities. Lesions on the head and neck only occasionally extend into the subcutis, whereas lesions on the trunk and extremities extend into the subcutis frequently. The overlying epidermis of the lesions on the head and neck are usually atrophic or ulcerated, and hyperkeratosis and parakeratosis is common. In contrast, the epidermis of lesions on the trunk and extremities is usually normal or acanthotic. Finally, the adjacent skin on the head and neck shows acinic damage, whereas adjacent skin on the trunk and extremities is often normal or acanthotic. Since AFX is mostly found in sun-exposed areas of the body, solar radiation very likely plays a key role in its pathogenesis. However, other possible causes are still being considered, such as X-ray radiation, burns, trauma, and a defective host immune response, especially in the non-sun-exposed clinical variant. Evidence that ultraviolet (UV) radiation plays a role in the development of AFX has been bolstered in the literature. UV radiation may mutate the p53 that can be present in AFX. Additional evidence is also found in xeroderma pigmentosum (XP)
patients, who have a defect in repair mechanisms of UV-induced DNA lesions. These patients may also have AFX in addition to sun-induced conditions like actinic keratosis, squamous cell carcinomas, and basal cell carcinomas. The presentation of AFX in a non-sun-exposed region, combined with histology demonstrating no actinic damage, is a reason to look for alternate causes and to consider UPS.

Immunosuppression is known to increase the incidence for SCC and BCC. For example, transplant recipients have an increased incidence of cancer presenting in the head and neck, and the vast majority of them are cutaneous in origin. This may lead some to assume that immunosuppression may also be a factor that would increase the incidence of AFX. With the true incidence of AFX unknown due to its rarity, establishing an increase in incidence may be difficult. One study mentioned only two AFX cases out of 8,724 (.023%) de novo malignancies in 8,191 solid-organ transplant recipients. A second study found one case of AFX out of 642 renal transplant recipients. The same study also found two cases of MFH (UPS). If AFX and UPS are considered the same, then the incidence may in fact be elevated in immunosuppressed patients. Finally, a third study did not mention AFX out of 484 cutaneous neoplasms in cardiothoracic transplant recipients. Although other substantially larger studies of AFX have been conducted, they did not specifically address immunosuppression as a factor.

AFX is thought to have a very low metastatic potential, with some favoring a diagnosis of superficial UPS for the rare instances of metastasis seen in patients diagnosed with AFX. Since there is a small chance of recurrence and metastasis, treatment of AFX requires surgical techniques such as Mohs micrographic surgery (MMS) or wide local incision (WLE). MMS seems to have a higher cure rate with fewer recurrences than WLE and allows for tissue sparing, making it the treatment of choice when possible. Follow-up for two years is recommended, with examination of the surgical site and palpation of the regional lymph nodes.

**Conclusion**

AFX typically presents in the sun-exposed areas of older white males, although a less common clinical variant presents in non-sun-exposed areas in a younger population. Epidemiology and histology differ between the clinical variants. The immunohistochemistry is important to help rule out other malignant cutaneous neoplasms. Although the prognosis is usually good, MMS is recommended for the small chance of recurrence or metastasis. Finally, the less common clinical variant may provide some insight into the causes of AFX and help with classification of AFX versus UPS.
References