Atypical Fibroxanthoma

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Abstract

Atypical fibroxanthoma (AFX) is a dermal spindle-cell sarcoma that is considered a superficial and clinically benign presentation of pleomorphic dermal sarcoma, malignant fibrous histiocytoma, and undifferentiated pleomorphic sarcoma. AFX appears clinically as a discrete red or pink nodule or papule, most commonly on the head and neck region of sun-damaged elderly patients. Histologic findings on routine hematoxylin and eosin staining reveal spindle-shaped, large, and pleomorphic tumor cells throughout the dermis. Immunohistochemistry is not specific for AFX, and the diagnosis is generally one of exclusion. AFX is best treated by complete surgical excision, with Mohs micrographic surgery considered the treatment of choice. Metastasis rarely occurs, but there is a high rate of local recurrence, especially in patients who are immunosuppressed.

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A typical fibroxanthoma (AFX) is an uncommon dermal spindle-cell tumor that typically occurs on the head and neck region of elderly patients. The estimated incidence of AFX is 1.8 cases per 100,000 people. Sun exposure plays an important role in the development of AFX, and p53 mutations have been described. Compared to other cutaneous malignancies, the nomenclature of AFX is confusing, and there is considerable overlap with pleomorphic dermal sarcoma (PDS), undifferentiated pleomorphic sarcoma (UPS), and malignant fibrous histiocytoma (MFH). In general, when a UPS arises within the dermis, it is referred to as MFH or PDS upon metastasis. Given this complexity in nomenclature, Winchester et al evaluated a large cohort of patients with any tumor in the above categories and, based on the risk of adverse outcomes, proposed subcategorization into superficial UPS and deep UPS relative to the superficial fascia.

For the purposes of this article, we will consistently use the term AFX to describe superficial UPS, the dermal-derived sarcomas.

FX appears clinically as a discrete red or pink nodule or papule (Figure), most commonly on the head and neck region of sun-damaged elderly patients. The tumor grows rapidly over the first several months but still retains a low risk for metastasis. Tumor behavior is predicted by invasion beyond subcutaneous fat, preoperative tumor size larger than 2 cm, immunosuppression, and the presence of lymphovascular invasion. In a recent systematic review, the metastatic rate from all case series and reports was determined to be less than 0.95%. Deaths associated with metastatic AFX are exceedingly rare, with less than 15 reported disease-related deaths in the literature.

Diagnosis

AFX is difficult to distinguish clinically from other cutaneous neoplasms. Physical examination of the non-specific pink or red nodule leads the examiner to consider other diagnoses such as pyogenic granuloma, squamous cell carcinoma (SCC), and melanoma. As such, a biopsy is critically important. Histopathologically, AFX is composed of spindle-shaped, large, and pleomorphic tumor cells confined to the upper dermis. In addition to AFX, the differential diagnosis of atypical spindle cells on hematoxylin and eosin confined to the dermis includes spindle-cell SCC, desmoplastic melanoma (DM), and leiomyosarcoma (LMS). Although immunohistochemistry (IHC) can aid in distinguishing these other atypical spindle-cell tumors of the dermis, AFX is still considered one of exclusion given lack of specific markers. Of note, procollagen 1 (PC1) is usually reactive in AFX, which supports further classification of this tumor being of fibrohistiocytic lineage. However, PC1 is not useful in diagnosis, as spindle-cell SCC, DM, and LMS can all show PC1 positivity. As such, reactivity with keratin, S100, and desmin should all be determined, as these will more specifically show IHC positivity with spindle-cell SCC, DM, and LMS, respectively. One must exert tremendous caution when interpreting S100 staining in AFXs, as S100-positive dendritic cells sometimes colonize the AFX lesion, but the neoplastic cells themselves are S100 negative, thereby excluding DM. Additionally, staining for histiocyes with CD163 and CD68 can be seen with AFX, although these stains are nonspecific with lower reactivity, further corroborating that AFX is a histopathologic diagnosis of exclusion.

There is scarce genetic information about AFX, but these tumors have been shown to harbor ultraviolet signature mutations and an RNA expression pattern similar to other soft tissue sarcomas. These tumors have upregulated gene signatures associated with epithelial to mesenchymal transition and tumor-associated macrophages, but they do not share mutational similarities with poorly differentiated SCC.

Radiologic imaging studies are only used when the tumor has metastasized or is not easily accessible, such as a subungual location. Magnetic resonance imaging of AFX on T1- and T2-
Treatment

Treatment of AFX is generally surgical, by wide local excision (WLE) or Mohs micrographic surgery (MMS). Tolkachjov et al performed a systematic review and meta-analysis of treatment of AFX with MMS or WLE. Their main finding was that MMS for AFX is associated with a lower recurrence rate than WLE, specifically a 2.0% recurrence rate with MMS versus 8.7% recurrence rate with WLE. Important considerations for treatment of AFX include the fact that immunocompromised patients have increased risk for recurrence, making MMS the treatment of choice for this patient population. Additionally, a higher rate of reported metastases were present in those tumors that had previously recurred, emphasizing the importance of complete tumor clearance during the first surgical procedure. The complete margin control made possible by MMS highlights why this is the treatment of choice for AFX.

Conclusion

AFX is an atypical spindle tumor cell proliferation confined to the upper dermis. Distinguishing AFX from spindle-cell SCC, DM, and LMS is impossible on hematoxylin and eosin alone and requires IHC staining to rule out these other conditions and make the diagnosis of exclusion. Staining with keratin, S100, and desmin should all be considered, as these will more specifically show IHC positivity with spindle-cell SCC, DM, and LMS, respectively, to aid in the diagnosis of AFX. Aggressive tumor behavior is predicted by invasion beyond subcutaneous fat, preoperative tumor size larger than 2 cm, immunosuppression, and the presence of lymphovascular invasion. Given that MMS is associated with a lower recurrence rate than WLE for AFX, and that metastases were most commonly reported in those tumors that had previously recurred, MMS remains the treatment of choice for AFX.

References