Angiofibroma of Soft Tissue: A Case Report

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Abstract

Angiofibroma of soft tissue, a newly described tumor that is essential not to miss.
Soft tissue tumors are rare tumors that arise from mesenchymal tissue. Based on the current World Health Organization (WHO) classification system, there are numerous types of soft tissue tumors, many of which have yet to be described. The diagnosis of soft tissue tumors is challenging, due in large part to the numerous types of these rare tumors and their similar morphological features. In contrast to most solid tumors which are typically categorized as benign or malignant, soft tissue tumors are categorized into, benign, intermediate and malignant.
With recent molecular advancements in medicine, the tumor subtype can be diagnosed, and in some cases, clinical behavior of tumors can be predicted. Additionally, with the discovery of new genetic abnormalities, tumor classifications are growing in number and many tumors that previously could not be classified are assigned to a new category each year.
Angiofibroma of soft tissue (AFST) is a benign, fibroblastic neoplasm composed of uniform spindle cells with abundant fibromyxoid stroma and a prominent network of innumerable branching, thin-walled blood vessels that shares morphological features with malignant and intermediate neoplasms. The accurate diagnosis of this tumor is essential to prevent unnecessary treatments and aggressive surgeries.
In this case report we share the diagnostic histological features as well as molecular/genetic findings. To the best of our knowledge, there are fewer than 50 cases of AFST that have been reported in the literature.

Introduction

Soft tissue tumors are rare and arise from mesenchymal tissue [1]. Based on the World Health Organization (WHO), there are many types of soft tissue tumors that exist, and these groups of tumors can be difficult to diagnose due to their similar morphological features [2]. Until recently, there was a lack of differentiating tests available to accurately diagnose the types of soft tissue tumors that exist, with an estimated inaccurate diagnoses made ranging between 20-30% [3]. In 2020, attempts to streamline the diagnosing process, the (WHO) thought it best to unify the roles of morphology and genetics to create a more accurate way to differentiate mesenchymal tumors [3].
Compared to solid tumors which are categorized as benign or malignant, soft tissue tumors are categorized into one of 3 categories: benign (low chance of recurrence), intermediate (high chance of local recurrence and minimal chance of metastasis) and malignant (high chance of metastasis). Angiofibroma of Soft Tissue (AFST) is a benign soft tissue tumor composed of uniform spindle cells with abundant fibromyxoid stroma and a strong network of vasculature made of extensive branching, thin-walled blood vessels [4]. The morphology of AFST is similar to some intermediate and malignant soft tissue tumors, however with the knowledge provided from the unification of genetics and morphology as detailed by WHO, diagnoses of AFST have become more precise [4].

Case Report

To the best of our knowledge, fewer than 50 cases of AFSTs have been reported in the literature with only several of those reported cases occurring in the back muscles. Here we present a newly described case of a benign, soft tissue tumor found within the back muscles of a 66-year-old man. After an initial diagnosis of malignant spindle cell neoplasm was made, the case was referred to our Sarcoma Department and the mass was excised. Intraoperatively, it appeared to be well encapsulated and was sitting in between the muscle bellies. On gross examination, the tumor was a well-circumscribed, heterogeneous mass, measuring 5.8 x 3.5 x 2 cm, composed of tan-brown to white-yellow cut surfaces with focal areas of hemorrhage and without definitive necrosis.
H&E sections show a well-circumscribed mass composed of relatively uniform, bland spindle cells within a variably myxoid-to-collagenous stroma, scattered lymphoplasmacytic infiltrates, and prominent and complex vascular pattern, some with hyalinized walls and fibrin depositions. (Figure 1-2) To further characterize these cells, immunohistochemical stains were performed; the neoplastic cells showed EMA (Figure 3) immunoreactivity with retained Rb nuclear staining, but negative for CD34 (Figure 4), Pan-cytokeratin, MUC4, SMA, Desmin, and S100 protein.
Overall, the clinical, histological, and immunohistochemical findings were most consistent with angiofibroma of soft tissue (AFST). To further characterize this lesion and confirm the diagnosis, we performed the UCSF500 cancer gene panel test, which revealed a pathogenic translocation involving AHRR, the gene encoding the aryl hydrocarbon receptor repressor, and NCOA2, the gene encoding the nuclear receptor coactivator 2. The translocation is predicted to create a chimeric protein where the N-terminus is composed of the AHRR protein (exons 1-10) and the C-terminus is composed of the NCOA2 protein (exons 13-23). Similar AHRR::NCOA2 fusions have been identified in the majority of angiofibroma of soft tissue 4, 9, 10 and have been shown to result in upregulation of the AHR/ARNT signaling pathway.

Histology

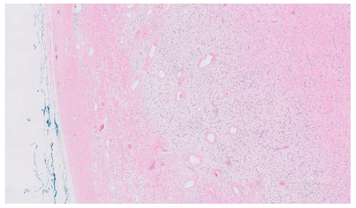

Figure 1: Photomicrograph of the mass (H&E stained, 100X magnification), showing well-circumscribed mass composed of hyalinized vessels and bland spindle cells within a fibromyxoid stroma.

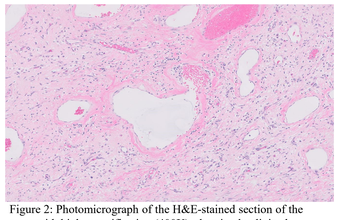

Figure 2: Photomicrograph of the H&E-stained section of the mass with high magnification (400X), showing hyalinized vessels, bland spindle cell cytomorphology, and scattered lymphocytic infiltrates.

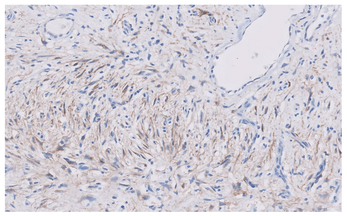

Figure 3: Photomicrograph of the EMA immunostain stained section of the mass, (400X magnification), showing positive immunoreactivity in spindle cells.

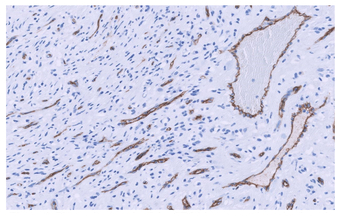

Figure 4: Photomicrograph of the CD34 immunostain stained section of the mass, (400X magnification), highlighting the vessels but negative immunoreactivity in spindle cells.

Discussion

Many cases of AFST are initially mistaken for low-grade sarcomas, solitary fibrous tumors, or other angiofibromatous tumors [4,5]. AFSTs typically occur in the soft tissue of extremities, primarily the lower extremities, with a preponderance toward middle aged adults and slight female predominance. These tumors can occasionally occur in the upper extremities, typically adjacent to a joint [5]. The current case is of particular interest and worthy of note because of the atypical location of the lesion on the back, though it did follow suit with other diagnostic characteristics. These lesions are considered slow growing and typically present as painless growths [5]. Surgical excision has been the standard treatment of choice for these lesions and includes a good prognosis [4]. Chances of local recurrence after resection with negative margins are rare and have only occurred in a few reported cases [5,6]. No metastases have been reported to date [8].
Genetic testing is an essential component of accurate diagnosis as the appearance of these lesions can mimic other, more harmful neoplasms. AFSTs often contain a unique NCOA2 fusion gene as well as other identifiable positive markers which include desmin, CD34, α-SMA, and epithelial membrane antigen [6-8]. Immunohistochemical analysis frequently shows the AHRR-NCOA2 driver mutation which is thought to be associated with t(5;8)(p15;q13), also commonly found in AFSTs [2]. One report found estrogen receptor and CD163 expression in immunostaining to be of particular importance in diagnosis of these lesions [6]. In combination, these immunohistochemical findings can improve accurate diagnosis of angiofibroma of soft tissue in any location of the body.

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