Angiomatoid Fibrous Histiocytoma: A Case Report and Review of the Literature

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ABSTRACT

Angiomatoid fibrous histiocytoma (AFH) is a rare soft tissue tumor most commonly occurring in children, adolescents, and young adults. Clinically and radiographically the lesion is easily confused with a hematoma, soft tissue hemangioma, or malignant fibrous histiocytoma. While the lesion is rare, due to the potential for local recurrence and metastasis, it is imperative to consider this lesion in the differential diagnosis of a soft tissue mass in a child or adolescent. Here, we present the clinical, radiologic, and pathologic findings of a case of AFH.

CASE REPORT

CASE REPORT

An 11 year-old girl presented with a painless mass in her right thigh for 2 months. She reported no constitutional symptoms. Physical exam demonstrated a mobile, nontender, palpable mass along the lateral aspect of the right thigh without erythema or soft tissue swelling. Following initial presentation, radiographs of the right thigh (Figure 1) exhibited an ovoid, soft tissue density mass, measuring 2.2 x 4.1 cm, projecting over the subcutaneous tissue of the lateral aspect of the right thigh, at the level of the distal femoral diaphysis.

Subsequent magnetic resonance (MR) imaging of the right thigh and knee (Figure 2) demonstrated a well-circumscribed, ovoid mass measuring 1.9 x 3.3 x 3.2 cm in the subcutaneous adipose tissue of the lateral, distal thigh abutting the vastus lateralis fascia but without involvement of the underlying musculature. The lesion was homogeneously hypointense on the T1WI and heterogeneously hyperintense on the T2WI with variegated internal and nodular peripheral gadolinium enhancement. Peripherally, a pseudocapsule was markedly hypointense on both T1- and T2WI showing a fine enhancement after gadolinium IV administration. There were two internal peripherally enhancing regions of iso-hypointensity on the T1WI and hyperintensity on T2WI in the anteriomedial aspect of the lesion representing either cystic components or hyperacute blood products. No fluid-fluid levels were detected. Multiple punctate foci of marked hypointensity markedly were scattered peripherally throughout the mass on the gradient echo sequences consistent with hemosiderin deposits. Hyperintensity was recognized to track minimally in the adjacent peritumoral fascial planes fat suppressed T2 weighted images representing edema.

The patient underwent en bloc surgical excision. On pathological examination, the lesion demonstrated characteristic features of AFH including multiple nodules of eosinophilic histiocytoid or more spindled cells associated with very prominent stromal hemorrhage, a dense hyaline fibrous pseudocapsule, and a peripheral lymphoplasmacytic infiltrate with germinal centers (Figure 3). The tumor cells showed strong positivity for desmin and multifocal positivity for epithelial membrane antigen (EMA) with no significant pleomorphism. Staging CT of the abdomen and pelvis 3 weeks after excision showed no evidence of metastasis and followup MR imaging 8 months after resection demonstrated small postoperative edema without evidence of recurrence.

DISCUSSION

When Enzinger initially described "angiomatoid malignant fibrous histiocytoma" in 1979 [1], the histogenesis was controversial. Today, the precise line of differentiation remains unknown, but this entity is no longer termed "malignant" due to its benign microscopic appearance and favorable prognosis [2]. Additionally, the 2002 World Health Organization (WHO) classification removed it from the malignant fibrous histiocytoma subtype of sarcoma (now synonymous with undifferentiated pleomorphic sarcoma) and placed it under the category of tumors of uncertain differentiation as angiomatoid fibrous histiocytoma [3].

AFH is a neoplasm that most commonly affects children and young adults, with a median age of 14 years. The tumor is rare, accounting for approximately 0.3% of all soft tissue neoplasms, albeit incidence may be underestimated due to overlapping histopathological findings [4,5]. Presentation usually involves a painless, slow growing mass within the deep dermis and subcutis [6]. It most commonly arises in sites of normal lymphoid tissue such as the antecubital fossa, axilla, inguinal and supraclavicular regions [3]. The majority of cases occur in the extremities, although cases have been reported in the head and neck region (10%) and trunk [1,7,8,9]. A small proportion of patients experience systemic symptoms including pyrexia, anemia, and malaise, suggesting tumoral cytokine production [10]. Symptoms of pain and tenderness are rarely encountered [11].

Making a pre-operative diagnosis of AFH is challenging with no distinct clinical or imaging findings to lead to diagnosis. Nonetheless, soft tissue malignancies have been stratified according to age and location to suggest one diagnosis more than another. For example, 80 % of of rare malignant soft tissue masses in a 6 - 15 year old patient in the hand and wrist, upper extremity, axilla and shoulder, lower extremity, hip, groin and buttocks, or trunk are either most likely or second most likely to be AFH according to a study of 39,179 soft tissue lesions over a 10 year period [12,13].

Despite this rigorous study, the imaging findings of AFH are as nonspecific as its histogenesis. When originating in the soft tissues, radiographs and computed tomography show a heterogeneous mass, and possibly hint at cystic and enhancing components, but ultimately are inferior to MR soft tissue detail. Consistent with the MR appearance in the 6 cases reported in the literature, our case also demonstrated (a) multiple internal cystic areas, (b) an enhancing fibrous pseudocapsule which was markedly hypointense on T1- and T2WI, and (c) foci of susceptibility artifacts representing hemosiderin. Conversely, inconsistent findings in the 6 previously reported cases included pattern of enhancement, if present or reported, and the presence, or absence of fluid-fluid levels. A summary and comparison of the findings in the cases are presented in Table 1. Taken together, these findings can be found with metastasis, hemangioma, hematoma, malignant fibrous histiocytoma, myxoid chondrosarcoma, leiomyosarcoma with necrosis, malignant ossifying fibromyxoid tumor, and various other sarcomas [14,15,16,17]. MR has traditionally been used for staging and followup, however a recent report highlights the potential utility of positron emission tomography in staging [18].

Given that AFH is histopathologically composed of blood/fluid-filled cystic spaces, the variability in enhancement is surprising. Presumably, this discrepancy arises due to fat suppression artifact in case 3 and the rare variant tissue of origin in case 5, bone. However, the variability of the presence of a fluid-fluid level is less confounding given that a it indicates tumoral hemorrhage, and therefore any variance can be attributed to differing ages of blood products [19,20,21].

The diagnosis of AFH is made based on histopathology and immunohistology. Macroscopically, AFH is generally firm and circumscribed. The characteristic microscopic appearance includes distributions of ovoid to spindle cells with bland, vesicular nuclei, lymphoplasmocytic infiltrate with intervening blood-filled cystic spaces, and a fibrous pseudocapsule [22,23]. Immunohistochemistry variably demonstrates positivity for desmin, CD68 and CD 99 [24]. Lastly, cytogenetic analysis has recently added to the diagnosis of AFH, with the EWSR1-CREB1 fusion gene present in the majority of AFH [4].

Since the tumor was originally described, many studies have been done to determine the malignant potential of AFH with varying conclusions. The cumulative findings of a meta-analysis of multiple studies demonstrate that the majority of patients (73.2%) are disease free after local excision and a minority (23.2%) develop recurrent disease and 8.7% develop metastatic disease within 24 months post operation [25]. The overall mortality rate is 4.3%, however maybe underestimated due to short follow-up periods [26]. While the tumor is often termed a low malignant potential lesion in the literature, it is officially classified as being of intermediate malignant potential [27,28,29]. The clinical behavior of the tumor cannot be determined based on clinical or histiologic parameters [6,30,31]. However, the development of both local recurrence and metastases has shown a correlation with invasion into the deep fascia or muscle as assessed surgically [30]. Treatment is surgical resection.

We report a case of AFH in the right thigh of a female adolescent. The case manifests the clinical, radiographic, and histopathologic features of AFH. The patient is free of recurrence following wide surgical excision approximately 30 months following surgery. Given the intermediate malignant potential of this lesion, the patient will require continued clinical and radiographic surveillance.

TEACHING POINT

Angiomatoid fibrous histiocytoma is a rare soft tissue tumor with intermediate malignant potential. While nonspecific, a mass with MR features including cystic areas, an enhancing fibrous pseudocapsule, and internal foci blood products in the extremity of a child or adolescent should prompt the consideration of AFH in the differential. Wide surgical excision with clear margins and post-excisional monitoring is warranted.

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FIGURES

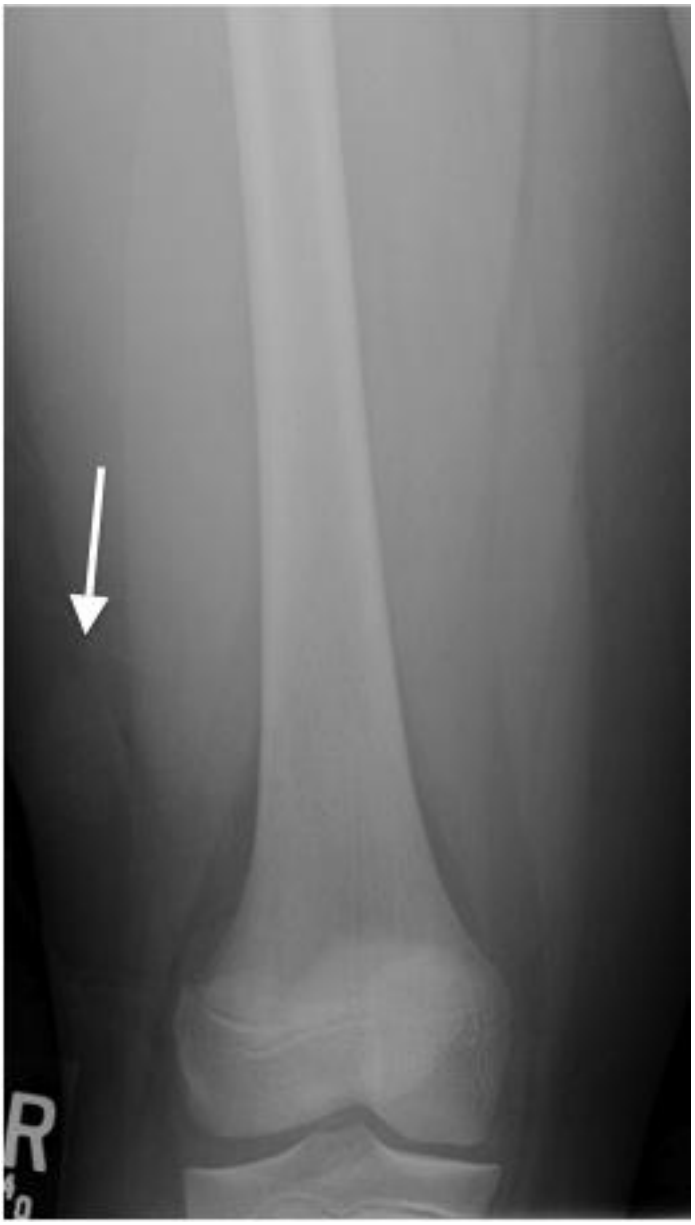

Figure 1: An 11 year-old girl with angiomatoid fibrous histiocytoma. Anteroposterior radiograph of the distal right thigh demonstrates a 2.2 x 4.1 cm well-circumscribed, ovoid mass in the soft tissue of the distal thigh, lateral to the distal femoral diaphysis.

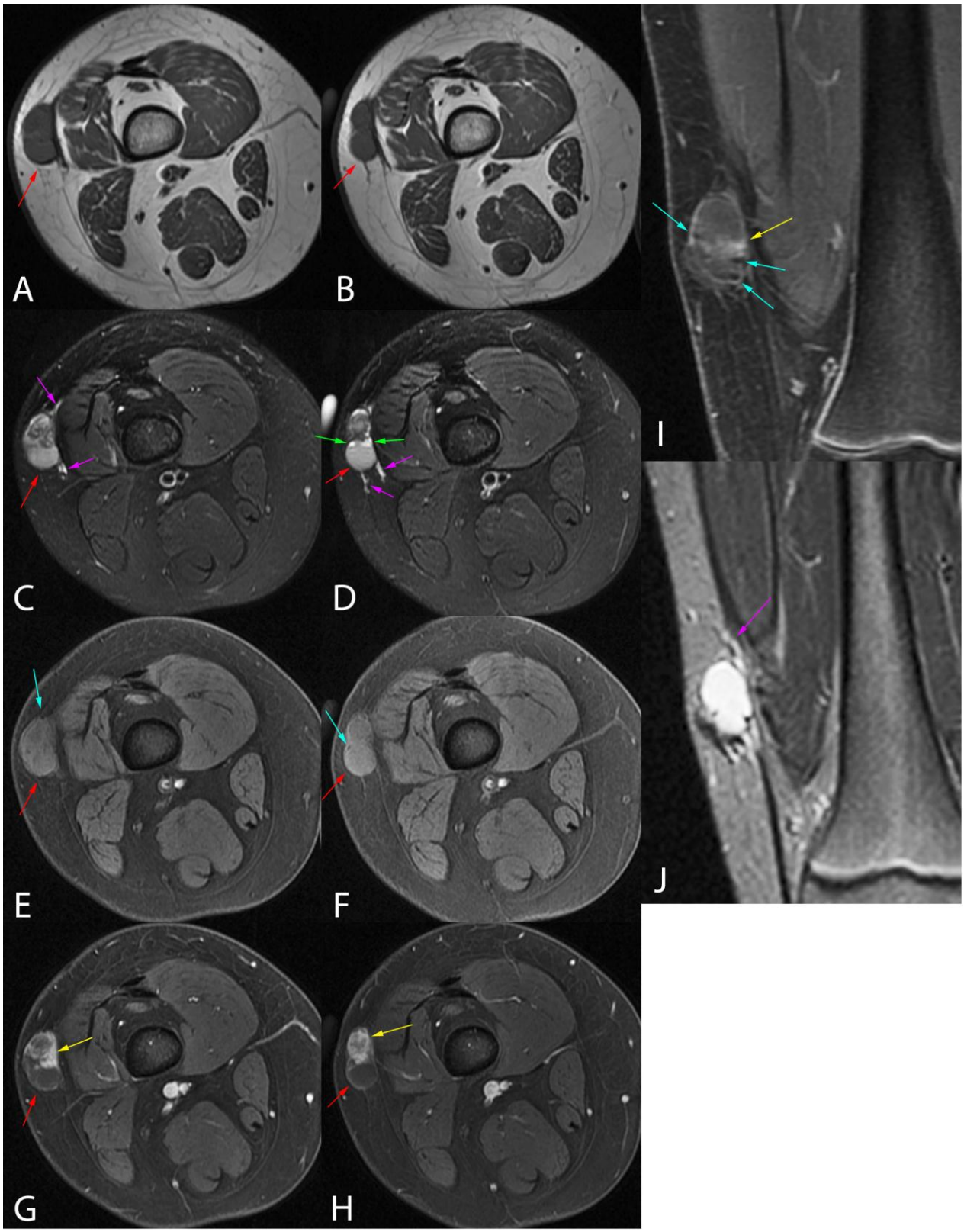

Figure 2: An 11 year-old girl with diagnosis of angiomatoid fibrous histiocytoma. 1.5 Tesla MR scanner axial (A,B) T1-weighted spin echo (TR 617 TE 11.5), (C,D) T2 fat suppressed spin echo (TR 3970, TE 71.3), (E,F) fat suppressed fast multiplanar gradient echo (TR 185, TE 2.27), (G,H,I) axial and coronal fat suppressed fast multiplanar gradient echo (TR 185, TE 2.27) with 16 mL of Magnevist intravenous contrast, (J) coronal STIR (TR 3100, TE 63.14) images. A 1.9 x 3.3 x 3.2 cm well-circumscribed, ovoid, mixed cystic (green arrows) and solid mass is present in the subcutaneous fat of the lateral, distal right thigh abutting the vastus lateralis fascia without evidence of muscle infiltration. The lesion is homogeneously hypointense (isointense to muscle) on the T1WI and heterogeneously hyperintense on the T2WI. The periphery of the mass demonstrates the typical low signal on nonenhanced images representing a fibrous pseudocapsule (red arrows). There is variegated and micronodular peripheral gadolinium enhancement (yellow arrows), as well as nodular peripheral foci of susceptibility artifact on gradient echo images (teal arrows). T2 hyperintensity tracks minimally in the adjacent peritumoral fascial planes representing edema (pink arrows).

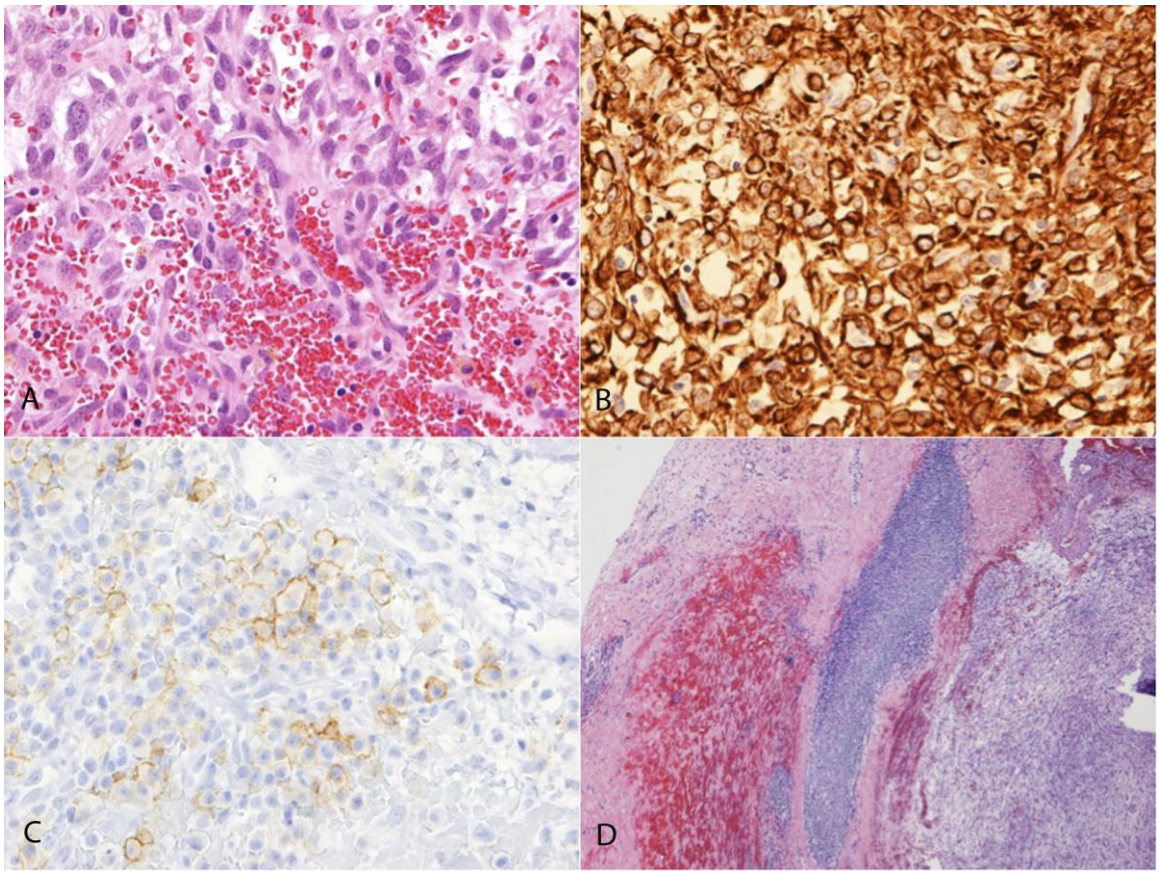

Figure 3: An 11 year-old girl with diagnosis of angiomatoid fibrous histiocytoma. H-E stain at 400x, 100x (A,D) , Desmin immunostain at 400x (B), and EMA immunostain at 400x (C). On pathological examination, the resection specimen demonstrated (A) areas of spindled cells and microscopic hemorrhage resembling vascular spaces, (B) diffuse positivity for desmin immunostain, (C) focal positivity for EMA immunostain, and (D) peripheral lymphoplasmacytic infiltrate with germinal centers within a dense hyaline fibrous pseudocapsule confirming a diagnosis of AFH.

	Aijlan et al.[32]		Li et al.[21]	Murphey et al.[15]	Petrey et al.[20] (osseous)	Mansfield et al.[33]	Bauer, Jackson, Gilbertson-Dahdal
Case #	1	2	3	4	5	6	7
Age (years)	28	85	32	10	5	25	11
Cystic areas	+	+	+	+	+	+	+
Pseudocapsule	+	+	+	+	+	+	+
Hemosiderin	+	+	+	?	+	+	+
Enhancement	Marked	Marked	-	?	Faint	Hetero +	Hetero +
Fluid-fluid level	+	-	+	+	+	?	-
T1	Homo iso	Homo iso	Homo iso	?	Homo iso	Iso	Homo iso
T2	Hyper	Hyper	Hetero iso/hyper	?	Hetero hyper	Hetero hyper	Hyper

Table 1: Imaging characteristics of reported AFH cases.

	Radiography	US	CT	MRI-T1	MRI-T2	Pattern of contrast enhancement	PET
Findings (AFH)	Soft tissue density in extremity	Soft tissue mass with heterogeneous echotexture +/- cystic spaces, fluid levels	Heterogeneous soft tissue mass in extremity isodense to muscle, high attenuation areas (corresponding with hemorrhage), hypodense areas corresponding to myxoid, necrosis, +/- cystic spaces, fluid levels	Homogeneously isointense to muscle on T1WI and correlating with pseudocapsule, +/- susceptibility artifact	Heterogeneously hyperintense, +/- susceptibility artifact, +/- cystic spaces, fluid levels, hypointense rim corresponding to pseudocapsule	Variegated and nodular peripheral gadolinium enhancement	Avid FDG uptake including lymph node metastasis
Differential Diagnosis - Adults	Malignant fibrous histiocytoma	Hematoma	Soft tissue sarcomas including MFH, fibrosarcoma, angiosarcoma	Soft tissue sarcomas including MFH, fibrosarcoma, angiosarcoma		Soft tissue sarcomas including MFH, fibrosarcoma, angiosarcoma	Soft tissue sarcomas including MFH, fibrosarcoma, angiosarcoma
	Fibrosarcoma	Soft tissue sarcomas	Muscle metastases	Muscle metastases		Muscle metastases	Muscle metastases
	Muscle metastases	Muscle metastases	Melanoma	Melanoma			Melanoma
	Hematoma	Benign lesions including lipoma, nerve sheath tumor, vascular anomalies					
	Nerve sheath tumor	Melanoma					
	Vascular anomalies						
	Melanoma						
Differential Diagnosis - Children	Malignant fibrous histiocytoma	Hematoma	Soft tissue sarcomas including MFH, angiosarcoma	Soft tissue sarcomas including MFH, angiosarcoma		Soft tissue sarcomas including MFH, angiosarcoma	Soft tissue sarcomas including MFH, angiosarcoma
	Extraosseous Ewing's	Soft tissue sarcomas	Muscle metastases	Muscle metastases		Muscle metastases	Muscle metastases
	Muscle metastases	Muscle metastases	Extraosseous Ewing's	Extraosseous Ewing's		Extraosseous Ewing's	Extraosseous Ewing's
	Hematoma	Benign lesions including lipoma, nerve sheath tumor, vascular anomalies					
	Nerve sheath tumor	Extraosseous Ewing's					
	Vascular anomalies						

Table 2: Differential Table of Angiomatoid Fibrous Histiocytoma

Etiology	Uncertain differentiation
Incidence	<< 1%, ~ 1/100,000; 0.3% of soft tissue neoplasms
Gender Ratio	1:3 F:M
Age Predilection	≤ 30
Risk Factors	None known
Treatment	Surgical excision
Prognosis	23% recurrence, 8.7 % metastasis; generally favorable but classified as intermediate biologic behavior
Findings on imaging	Soft tissue mass in extremity, heterogeneous density, echogenicity, T1,T2 signal, with hemorrhage, myxoid, necrosis, +/- cystic spaces, fluid levels

Table 3: Summary Table of Angiomatoid Fibrous Histiocytoma

ABBREVIATIONS

AFH = angiomatoid fibrous histiocytoma
EMA = epithelial membrane antigen
H-E = Haematoxylin Eosin
MR = magnetic resonance
STIR = short tau inversion recovery
T1WI = T1-weighted image
T2WI = T2-weighted image
WHO = World Health Organization

KEYWORDS

Angiomatoid fibrous histiocytoma; soft tissue neoplasm