


Difficult diagnosis of Angiomatoid Fibrous Histiocytoma of the leg mimicking a benign condition

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ABSTRACT

Angiomatoid fibrous histiocytoma is a rarely metastasizing soft-tissue tumor of low-grade malignancy. Here we report a case of angiomatoid fibrous histiocytoma located in the leg of a 15-year-old female. This case is of particular interest due to its radiological features that led to raise two questions concerning the nature of the disease (is it reactive or tumoral?) and its site of origin (within soft tissues or the tibial periosteum?). Here we describe ultrasound, magnetic resonance imaging, computed tomography scan and positron emission tomography findings that helped answer these questions, understand the real nature of the disease and its appropriate treatment. This case shows that a single type of imaging technique may not be sufficient to understand the real nature of a musculoskeletal lesion and that it is necessary to combine all information derived from various imaging techniques in order to correctly diagnose and treat the disease.

CASE REPORT

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A 15-year-old female was admitted to our hospital complaining of a small swelling on the left leg that had been present for approximately 40 days. The patient reported minor trauma in the affected leg four weeks prior to the appearance of the swelling.

Physical examination revealed local swelling without tenderness to palpation and no spontaneous pain. The patient was able to walk and run freely although she experienced occasional discomfort. Constitutional symptoms such as fever or weight loss were absent and the skin around the swelling was normal, neither red nor warm.

Routine laboratory tests were within the norm: blood count, alkaline phosphatase, lactate dehydrogenase, C-reactive protein and erythrocyte sedimentation rate were all normal.

Magnetic resonance imaging (MRI) of the leg in question revealed the presence of a small round lesion (maximum cranio-caudal diameter of 18 mm; maximum axial diameters of 14.5x17 mm) closely contiguous to the cortical bone of the tibia with the following features: mildly hyperintense compared to the muscle in T1- and T2-weighted sequences (Fig. 1), markedly hyperintense at the periphery compared to the center with polylobate margins in proton-density (PD) fat-saturated images (Fig. 2) and homogeneously but moderately hyperintense in short-tau inversion recovery (STIR) sequences (Fig. 3). This aspect suggested a mixed lesion with solid and

fluid components but posed two questions: 1) Did the lesion arise from the soft tissues or from the tibial periosteum? Or 2) Was it a reactive (hematoma, hemangioma) or a neoplastic lesion?

Considering the limited symptoms reported by the patient and the small size of the lesion, we decided to perform an ultrasound two months later followed by another MRI four months later with no other medical or surgical interventions.

The subsequent ultrasound showed a 3 cm hypoechogenic expansive lesion (Fig. 4). The second MRI was very interesting because the lesion had changed in shape and increased in size: from round to hourglass with a maximum cranio-caudal diameter of 50 mm and maximum axial diameters of 20x20 mm. Furthermore, the lesion presented the following signal intensity features: the distal component was markedly and homogeneously hyperintense (cranio-caudal diameter 35 mm), and the proximal component was moderately and homogeneously hyperintense (cranio-caudal diameter 15 mm) in T1-weighted sequences. In T2-weighted sequences both parts of the lesion were homogeneously and mildly hyperintense but with the presence of a fluid-fluid level in the proximal component (Fig. 5). In STIR sequences the distal component was moderately and homogeneously hyperintense, and the proximal component markedly and homogeneously hyperintense (Fig. 6). These radiological features confirmed the mixed nature of the lesion that seemed to have a blood component. The tibial periosteum appeared thickened (Fig. 7) and this aspect led to some doubts about the origin of the lesion (soft tissues versus bone). A 18-fluorodeoxyglucose (FDG) positron emission tomography with CT (PET/CT) was thus performed showing an uptake in the soft tissue of the leg where the lesion was present (SUVmax 3.2) without bone involvement (Fig. 8).

Considering the increase in size of the lesion, we decided to perform an incisional biopsy with the intention of providing a definitive histological diagnosis. The histological diagnosis (Fig.9) was angiomatoid fibrous histiocytoma (AFH).

Three months later another MRI was performed, with the same weighted sequences, and which did not reveal any changes in size or signal intensity of the lesion. A surgical excision of the lesion was performed the next day. Histological examination of the surgical specimen confirmed the diagnosis of AFH. The surgical margins were wide and no evidence of disease was present at the 18-month follow-up.

Clinical & Imaging Findings:

Clinical and radiological aspects of the disease are non-specific including painless, slow-growing masses that by MRI present cystic areas with an enhancing fibrous pseudocapsule and internal blood-filled foci [5, 6]. At initial presentation, AFHs are surrounded by a low signal intensity fibrous pseudocapsule. High signal intensity consistent with the lymphoplasmacytic infiltrate was seen in T2-weighted and post-contrast images as a rim over the hypointense pseudocapsule (double rim sign). The lack of peculiar radiological features and the slow clinical course of the disease makes diagnosis difficult [7].

Differential Diagnosis:

There are no specific radiological features that differentiate this tumor from other clinical entities, but all the clinical and radiological data evaluated during follow-up allow to suspect the disease. Possible differential diagnoses include several entities ranging from reactive lesions to malignant tumors (Table 2): hematoma, hemangioma, synovial sarcoma, myxofibrosarcoma, nodular Kaposi sarcoma and other soft tissue sarcomas [5, 8, 9]. Diagnosis of AFH must be confirmed by histology and genetic analysis. In fact, AFH can be associated with three translocations: t(2:22)(q33;q12) (forming the EWSR1-CREB1 fusion gene), t(12:22)(q13;q12) (forming the EWSR1-ATF1 fusion gene) and t(12:16)(q13;p11) (resulting in the FUS-ATF1 fusion gene) [2, 10, 11]. In our case, for example, the neoplastic cells showed a positivity for smooth muscle actin and desmin and were negative for S100 protein, for epithelial markers (cytokeratin AE1/AE3 and MNF116), for vascular markers (ERG and CD31) and for follicular dendritic cell markers (CD21 and CD35). FISH analysis on the histological section showed rearrangement of the EWSR1 gene confirming the morphological and immunohistochemical diagnosis.

Treatment & Prognosis:

Wide surgical excision and thorough follow-ups are recommended in the treatment of AFH [5, 8] (Table 1). After the excision it is important to continue with thorough clinical and radiological follow-ups because of the risk of local recurrence and distant metastases [1, 8]. Chemotherapy and radiotherapy are rarely used but can be useful in the event of distant metastases and/or multiple local recurrences [12, 13].

DISCUSSION

Etiology & Demographics:

Angiomatoid fibrous histiocytoma (AFH) is a rare soft tissue tumor with uncertain histogenesis that mostly affects children and young adults and frequently involves superficial soft tissue of the extremities [1, 2]. It represents 0.3% of all soft tissue tumors (Table 1) and is classified by the World Health Organization (WHO). AFH has a local recurrence rate of 15-20% and a percentage of distant metastases of 1-3% [3, 4, 5].

TEACHING POINT

Although non-specific, magnetic resonance imaging features of angiomatoid fibrous histiocytoma include: cystic areas, an enhancing fibrous pseudocapsule and internal foci blood products located at the extremities usually in children/adolescents. In musculoskeletal lesions the presence of these signs should prompt considering angiomatoid fibrous histiocytoma in the differential diagnosis, especially when the size of a lesion grows over time, even if its initial radiological features appear non-aggressive. Wide surgical excision and

thorough follow-ups are recommended in the management of this disease.

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FIGURES



Figure 1: A 15-year-old female with angiomatoid fibrous histiocytoma of the leg.

Findings: Coronal T1-weighted MR imaging showed the presence of a small lesion (less than 2cm) closely contiguous to the cortical bone of the tibia, highly hyperintense compared to the muscle (arrow).

Technique: 1,5 Tesla Magnet, Coronal T1-weighted image.

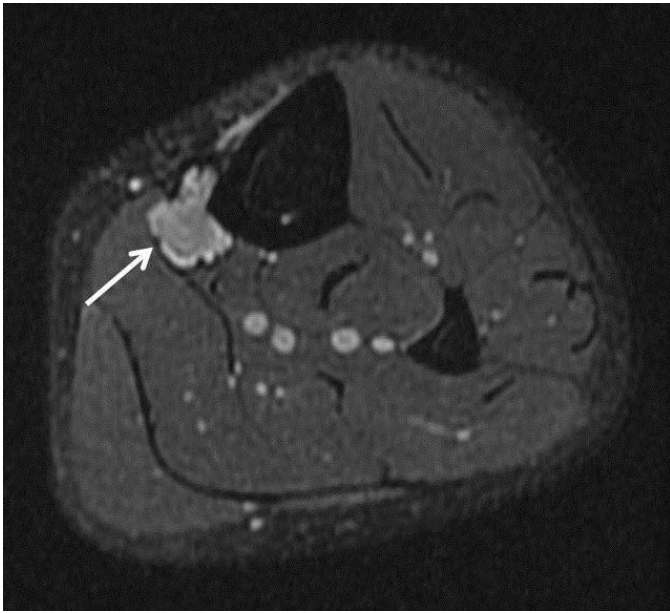


Figure 2: A 15-year-old female with angiomatoid fibrous histiocytoma of the leg.
Findings: Axial proton-density (PD) fat saturated MR imaging confirmed the presence of a lesion that was highly hyperintense more at the periphery than at the center with polylobate margins (arrow).
Technique: 1,5 Tesla Magnet, Axial proton-density (PD) fat saturated image.

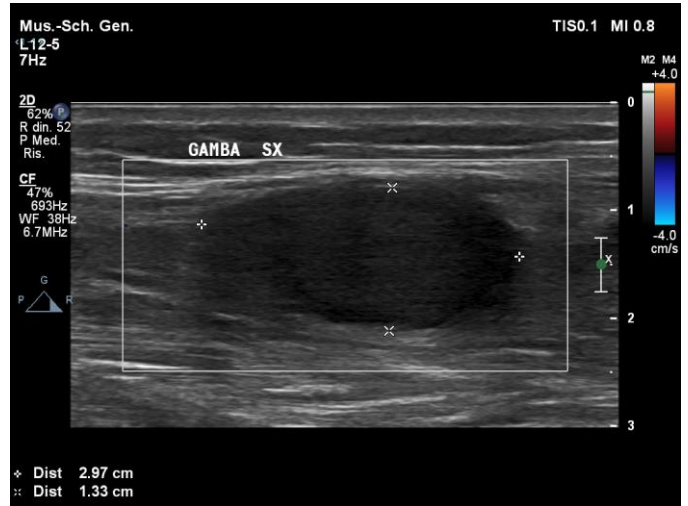


Figure 4: A 15-year-old female with angiomatoid fibrous histiocytoma of the leg.
Findings: Ultrasound shows hypoechoic lesion (maximum diameter 3cm); color-power Doppler evaluation does not show any sign of vascularization within the lesion.
Technique: Ultrasound has been performed with 12 Mhz linear probe, soft-tissue settings.

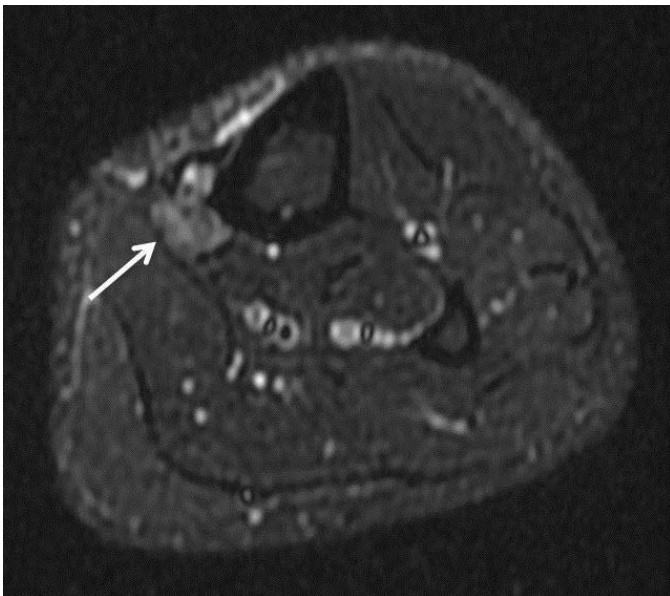


Figure 3: A 15-year-old female with angiomatoid fibrous histiocytoma of the leg.
Findings: Axial STIR sequence MR imaging showed a homogeneously but moderately hyperintense lesion contiguous to the tibia (arrow).
Technique: 1,5 Tesla Magnet, Axial STIR sequence image.

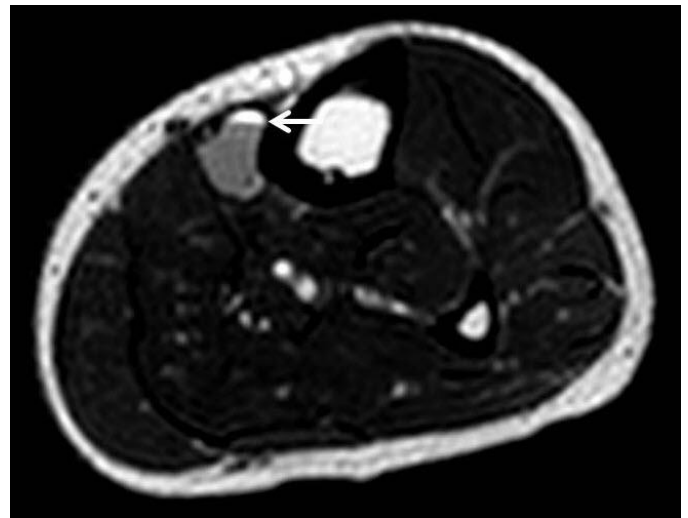


Figure 5: A 15-year-old female with angiomatoid fibrous histiocytoma of the leg.
Findings: Axial T2-weighted sequence MR imaging, performed four months after the first, showed the presence of a fluid-fluid level (arrow) in the proximal component suggesting the presence of a blood component in the lesion.
Technique: 1,5 Tesla Magnet, Axial T2-weighted image.



Figure 6 (left): A 15-year-old female with angiomatoid fibrous histiocytoma of the leg.

Findings: Coronal STIR MR imaging, performed four months after the first, showed an increase in size of the lesion (cranio-caudal diameter of 50mm); the lesion assumed an hourglass shape and resulted moderately and homogeneously hyperintense in the distal component (arrow) and markedly and homogeneously hyperintense in the proximal component (dotted arrow).

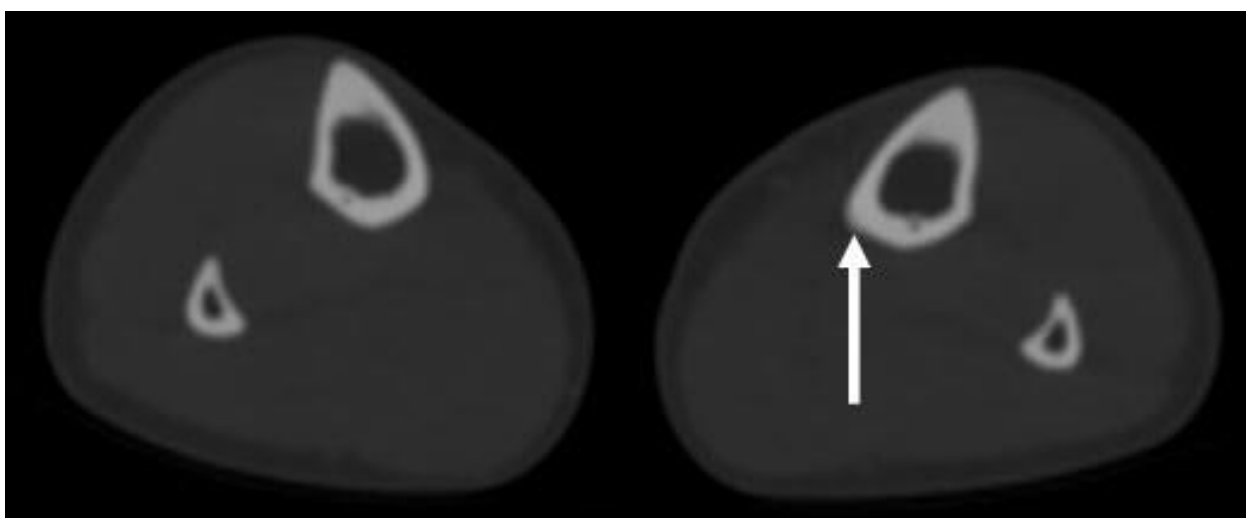
Technique: 1,5 Tesla Magnet, Coronal STIR image.

Figure 7 (bottom): A 15-year-old female with angiomatoid fibrous histiocytoma of the leg.

Findings: Computed tomography images (obtained from PET-CT studies) showed sharp periosteal thickening at the medial profile of the left tibia (arrow).

Technique: Computed tomography images (obtained from PET-CT studies).

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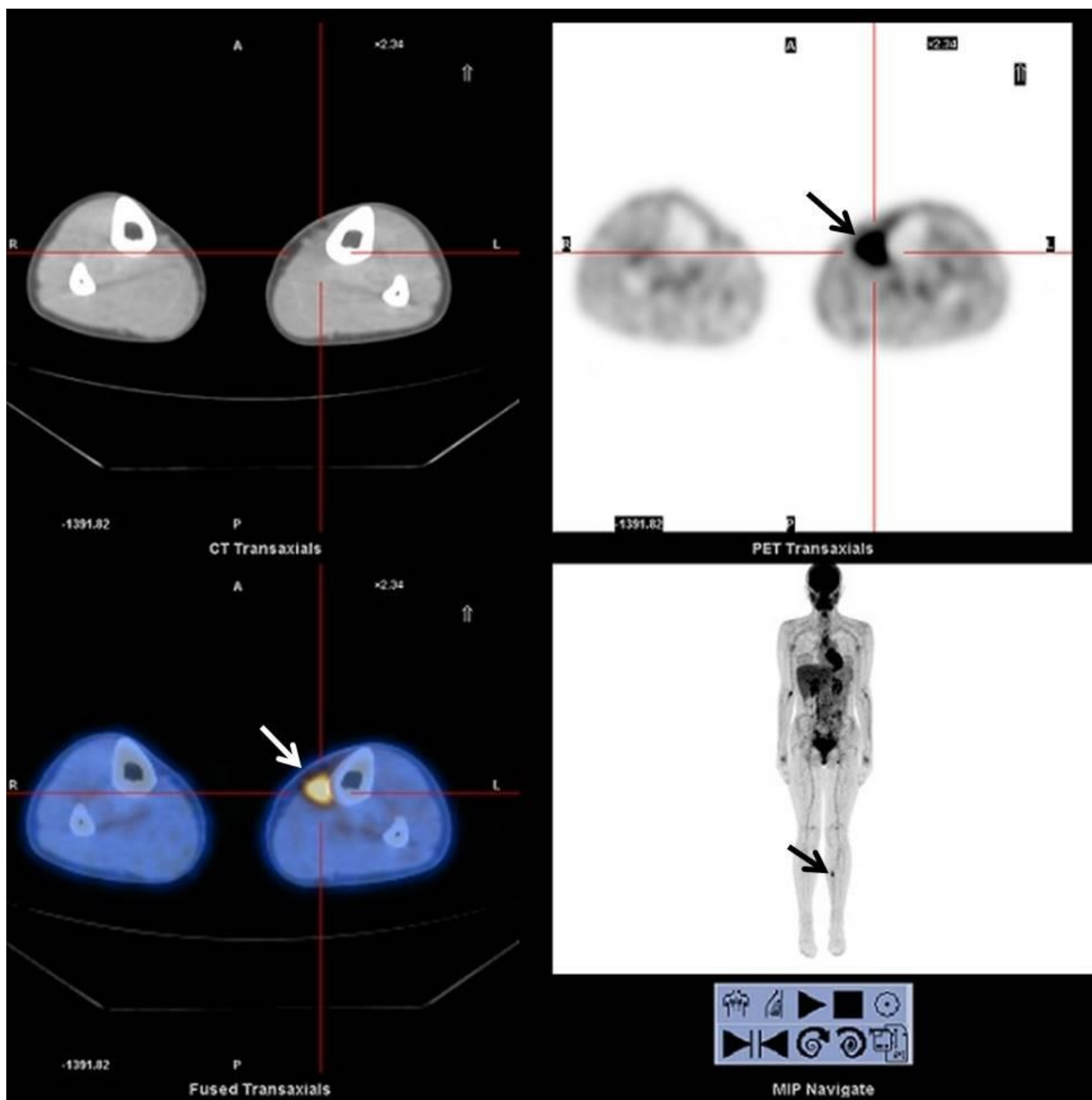


Figure 8: A 15-year-old female with angiomatoid fibrous histiocytoma of the leg. Findings: 18-FDG PET/CT fused images, performed six months after the first MRI, showed an uptake in the soft tissue of the leg (SUVmax 3.2) without bone involvement (arrows). Technique: patient received 3.7 MBq/kg of ¹⁸F-FDG intravenously and the PET/CT scan was performed 60-90 min after tracer administration. PET emission images were collected for 2 min for each bed position from the vertex of the skull to the thighs with inclusion of the upper extremities, and the CT scan was used for non-uniform attenuation correction. CT acquisition parameters were: 120 kV, 80 mA, 0.8 s tube rotation, 3.7 mm slice thickness.

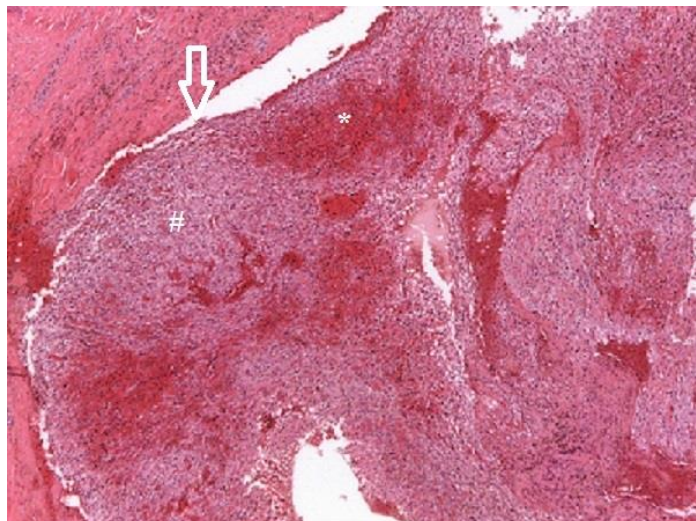


Figure 9 (left): A 15-year-old female with angiomatoid fibrous histiocytoma of the leg. Findings: Haematoxylin and eosin staining highlights the neoplasm composed histiocyte-like (#) or short spindled myoid cells (*) surrounded by a thick fibrous capsule (arrow) (100X magnification).

Etiology	Unknown
Incidence	0.3% of all soft tissue tumors
Gender ratio	Slight male predominance
Age predilection	Children and young adults (<30 years old)
Risk factors	Unknown
Treatment	Wide surgical excision
Prognosis	Good (percentage of distant metastases of 1-3%)

Table 1: Summary table of Angiomatoid Fibrous Histiocytoma.

	Ultrasound	MRI	Pattern of contrast enhancement	PET
AFH	Heterogeneous echotexture (prevalent hypoechoic lesion) with cystic spaces and fluid levels	Mildly hyperintense compared to the muscle in T1 sequences; heterogeneously hyperintense in T2 sequences where cystic spaces and fluid levels can be observed.	Variegated and nodular peripheral gadolinium enhancement	Moderate uptake.
Hematoma	Cystic-like mass with anechoic appearance.	Cystic-like mass with high heterogeneous signal intensity on T1 and T2-weighted images.	None, except for hematoma with active bleeding.	No uptake.
Hemangioma	Hyperechoic. Calcifications can be detected.	T1 isointense; T2 hyperintense.	Centripetal fill.	Moderate uptake.
Synovial Sarcoma	Non-specific findings. Usually the appearance consists in a heterogeneous predominantly hypoechoic mass.	Non-specific findings. T1 iso- (slightly hyper-) intense heterogeneous. T2 mostly hyperintense.	Noticeable and can be diffuse, heterogeneous, or peripheral.	Mild uptake.
Myxofibrosarcoma	Myxoid component usually appears as cystic-like mass, anechoic. Other features may be non-specific.	T1 low signal (myxoid component). T2/STIR high signal (myxoid component). Other features may be non-specific.	The myxoid component tends not to enhance or mildly so, while the remaining soft tissue component enhances.	Variable.
Kaposi sarcoma	Hyperechoic/heterogeneous	T1 usually hypointense. T2 usually hyperintense.	Conspicuous enhancement.	Variable.

Table 2: Differential diagnoses table for Angiomatoid Fibrous Histiocytoma.

ABBREVIATIONS

AFH = Angiomatoid fibrous histiocytoma
 FDG = Fluorodeoxyglucose
 MRI = Magnetic resonance imaging
 PD = Proton-density
 PET = Positron emission tomography
 STIR = Short-tau inversion recovery
 WHO = World Health Organization

KEYWORDS

Angiomatoid Fibrous Histiocytoma; soft tissue tumors; MRI; 18-FDG PET/CT; EWSR1-CREB1 fusion gene

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