

Clinical and Radiological Spectrum of Angiomatoid Fibrous Histiocytoma of the Musculoskeletal System: A Case Series

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ABSTRACT

Angiomatoid Fibrous Histiocytoma (AFH) represents a rare and clinically deceptive mesenchymal neoplasm that primarily affects children and young adults. Currently, classified by the World Health Organisation (WHO) as a tumour of intermediate malignant potential, AFH is frequently characterised by an indolent clinical course; however, it presents a formidable diagnostic challenge due to its profound clinical and radiological heterogeneity. The Magnetic Resonance Imaging (MRI) features described are multiple internal blood-fluid levels, a T2-hypointense fibrous pseudocapsule, focal nodularity along the cyst wall, and the double rim sign. Definitive diagnosis rests upon histopathological confirmation and molecular testing for the pathognomonic EWSR1-CREB1 fusion. The primary management strategy is centred on wide local surgical excision. In this series, authors describe a heterogeneous group of clinical and radiological presentations of this entity within bone and muscle, ranging from superficial, well-circumscribed soft-tissue masses to aggressive, bone-eroding lesions. These varied cases highlight the absolute necessity of maintaining a high-index of clinical suspicion for AFH when evaluating any recurrent or atypical cystic musculoskeletal lesion.

Keywords: Diagnosis, Haematoma, Haemosiderin deposition, Mesenchymal neoplasm, Musculoskeletal

INTRODUCTION

The AFH is a rare soft-tissue mesenchymal neoplasm of uncertain histogenesis and line of differentiation that most commonly affects children and young adults. Currently, it is no longer regarded as “malignant” because of its benign microscopic appearance and favourable prognosis. In the 2020 WHO classification, AFH are classified as “intermediate tumours of uncertain differentiation [1].

CASE SERIES

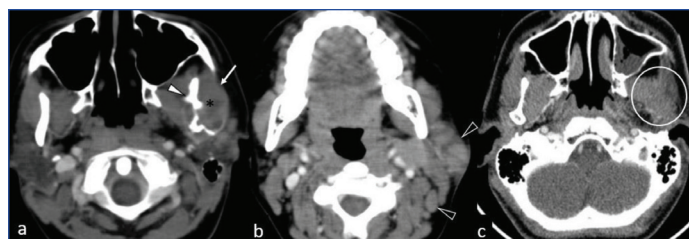
Case 1

A 16-year-old male patient presented to the head and neck surgery Outpatient Department (OPD) with a five-month history of painless left facial swelling and intermittent low-grade fever. Following an inconclusive biopsy elsewhere, empirical antibiotics were given for suspected infection, but there was no subsequent clinical improvement. Physical examination revealed an ill-defined, 4x4 cm, firm, painless, left preauricular mass with a serous-discharging scar from the site of previous intervention, suggestive of a salivary fistula. Firm cervical (levels I and II) and post-auricular lymphadenopathy were present, alongside signs of partial left-sided facial nerve palsy.

Initial laboratory investigations revealed anaemia (haemoglobin 7 g/dL), with normal leucocyte counts (4,600/ μ L) and C-Reactive Protein (CRP <6 mg/L). Given the fever, anaemia, and lymphadenopathy, a lymphoproliferative disorder was initially suspected; Positron Emission Tomography-Computed Tomography (PET-CT) [Table/Fig-1a,b] demonstrated an expansile lytic lesion of the left mandibular ramus with an enhancing soft-tissue component infiltrating the masseter muscle and associated large left-sided cervical and post-auricular lymph nodes (up to 17 mm). An aggressive primary bone lesion and lymphoma were considered differentials in view of the infiltrative soft-tissue component with nodal mass. Langerhans' cell histiocytosis was a close differential in this age group; however, the presence of nodal mass went against this diagnosis. Osteosarcoma

was considered less likely due to the absence of osteoid matrix and Ewing's sarcoma of the jaw is rare. Infection was considered less likely due to the absence of collections and significant fat stranding. Cervical lymph node biopsy demonstrated reactive follicular hyperplasia and bone marrow biopsy was normal, effectively ruling out lymphoma. Incisional biopsy of the mandibular lesion showed sheets of histiocytoid spindle cells within a fibrotic stroma containing perivascular lymphocytic aggregates, producing a pseudoangiomatous pattern. A thick pseudocapsule with moderate lymphoplasmacytic infiltrate surrounded the tumour- features consistent with AFH.

Following multidisciplinary review, the patient underwent definitive surgery including wide local excision, posterior segmental mandibulectomy, Infratemporal Fossa (ITF) clearance, and modified radical neck dissection with a Pectoralis Major Myocutaneous (PMMC) flap. Final histopathology confirmed AFH with infiltration of adjacent skeletal muscle and fibroadipose tissue, and the lymph nodes were free of tumour. Adjuvant radiotherapy was administered due to local invasion. At one-year follow-up, the patient showed complete clinical and radiological resolution with no evidence of recurrence [Table/Fig-1c].



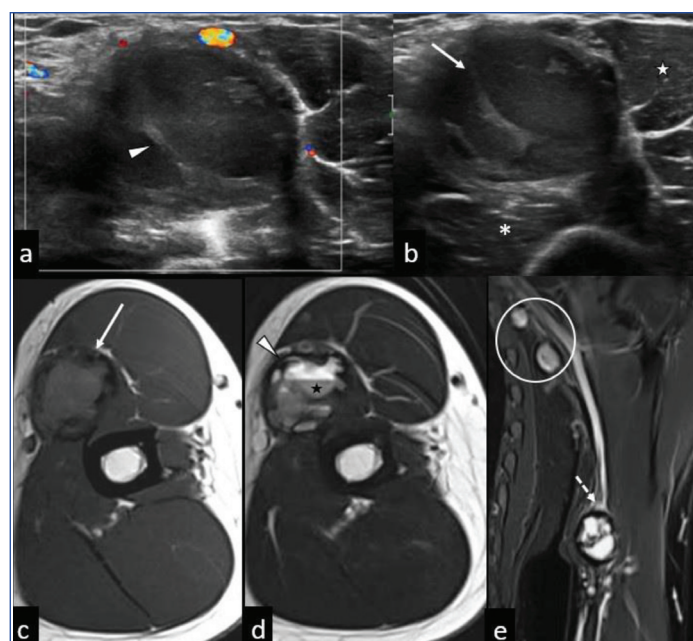
[Table/Fig-1]: CT axial images obtained as part of PET/CT: (a,b) Shows an expansile lytic lesion involving the left mandibular ramus (white arrowhead), with an enhancing soft-tissue component (asterisk) infiltrating the masseter muscle (arrow), along with enlarged left cervical and postauricular lymph nodes (black arrowheads). One-year follow-up contrast-enhanced CT axial section; (c) shows postoperative changes without any enhancing lesion to suggest recurrence (circle).

Case 2

A 32-year-old male patient initially presented to the hand surgery OPD for repair of a post-traumatic brachial plexus injury after a fall from a bike three months ago. Concurrently, he reported a gradually progressive swelling on the medial aspect of the contralateral (left) arm for two years. Physical examination revealed no visible swelling; however, deep palpation identified a 3×2 cm, firm, solid, and painless mass along the inner aspect of the arm, with no local warmth, tenderness, skin discolouration, pulsatility, or bruit. There was full range of motion at the shoulder joint, with no neurological deficits or features of vascular compromise. Laboratory investigations were unremarkable. Given his history of trauma, clinical differentials included an organising haematoma or brachialis muscle rupture.

The ultrasound demonstrated a 2×2×3 cm, circumscribed, heteroechoic, cystic lesion with posterior acoustic enhancement and thick internal septations in the intermuscular plane between the biceps and brachialis muscles [Table/Fig-2]. The lesion contained mobile internal echoes without internal vascularity or definite solid component, which favoured a chronic haematoma over a mass lesion. An organised abscess would have been a close differential; however, there was no local warmth, tenderness, fever, or leucocytosis to support the same. In view of the imaging findings combined with the history of prior trauma, a possible chronic haematoma was considered likely. Patient was given conservative management, which consisted of rest and advice to follow up if symptoms worsened. He presented one year later with a painful, progressive increase in the size of the mass.

Subsequent MRI revealed a well-defined, multiloculated cystic lesion with blood-fluid levels and a T2-hypointense rim, accompanied by mild perilesional oedema [Table/Fig-2]. The lesion had mildly increased in size from prior Ultrasonography (USG), measuring 3×3.5×2.5 cm. No regional lymphadenopathy was identified. While the mass closely abutted the brachial vessels and median nerve, there was no evidence of direct soft-tissue infiltration. Based on these imaging features, a soft-tissue tumour, potentially of vascular origin, was suspected. The patient underwent complete surgical excision, and histopathology confirmed the diagnosis of AFH. The patient was reviewed after four years, remained symptom-free, and



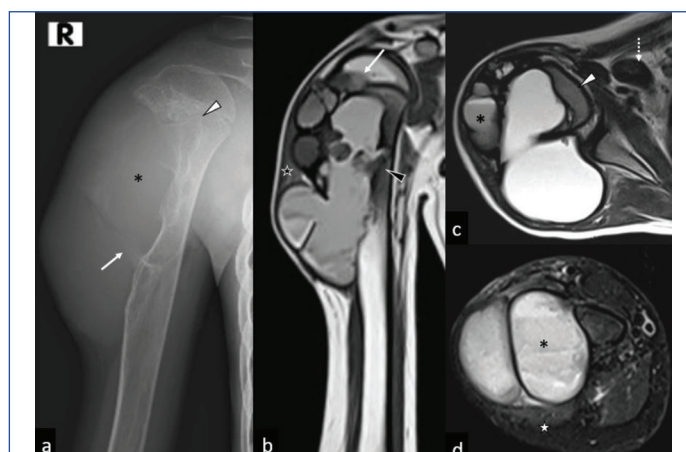
[Table/Fig-2]: Ultrasound images (a,b) demonstrate a well-circumscribed cystic lesion (arrow) with mobile internal echoes and thick internal septations (arrowhead), located in the intermuscular plane between the biceps (star) and brachialis muscles (asterisk), without internal vascularity; (c) MRI, including axial T1-weighted (d) axial T2-weighted and (e) coronal STIR images, shows a well-defined multiloculated cystic lesion (arrow) with blood-fluid levels (star) and a T2-hypointense rim (arrowhead), associated with mild perilesional oedema (dotted arrow). Enlarged axillary lymph nodes are also noted (circle).

had no recurrent swelling on examination. He was advised to get a reassessment MRI, which he opted to do at his hometown.

Case 3

A 14-year-old male presented to the paediatric orthopaedics OPD with a six-month history of painful swelling in the right proximal arm. There were no associated constitutional symptoms, such as fever or weight loss. A biopsy performed prior to referral had suggested chronic osteomyelitis. Physical examination revealed a 20×10 cm, warm, palpable mass over the anterolateral aspect of the proximal humerus. Laboratory investigations, including haemoglobin (13.5 g/dL), total leucocyte count (4,600/μL), and CRP (<3 mg/L), were unremarkable.

Plain radiographs showed a large, expansile, eccentric lytic lesion arising from the proximal humeral metadiaphysis measuring 13×6×7 cm [Table/Fig-3]. The lesion exhibited permeative bone destruction and a discontinuous periosteal reaction, notably lacking matrix mineralization. Subsequent MRI characterised the mass as a large, multiloculated cystic lesion featuring T2-hypointense solid components and prominent blood-fluid levels [Table/Fig-3]. Focal transphyseal extension and perilesional marrow oedema were observed, with evidence of infiltration into the overlying deltoid and the medial head of the triceps. Multiple ipsilateral axillary lymph nodes were also identified. Given the aggressive radiological features and significant haemorrhagic components, telangiectatic osteosarcoma was considered the primary differential diagnosis. However, a core needle biopsy revealed a spindle cell neoplasm with cellular atypia, and the immunoprofile suggested AFH.



[Table/Fig-3]: (a) Plain radiograph demonstrates a large, expansile, eccentric lytic lesion (asterisk) arising from the proximal humeral metadiaphysis, with permeative bone destruction (arrowhead), discontinuous periosteal reaction (arrow), and no matrix mineralisation. MRI of the right arm, including coronal T1-weighted; (b) Axial T1-weighted; (c) and axial STIR; (d) Images, demonstrates a large multiloculated cystic lesion with T2-hypointense solid components (arrowhead) and prominent blood-fluid levels (asterisk). There is focal transphyseal extension (arrow), perilesional marrow oedema (black arrowhead), and infiltration into the overlying deltoid (star) and medial head of the triceps (star). Multiple ipsilateral axillary lymph nodes are also present (dotted arrow).

The patient underwent wide tumour resection and biological reconstruction using an ipsilateral free vascularised fibula graft. The pathology report was consistent with AFH with adequate surgical margins, and the lymph nodes were free of tumour. Hence, the patient was kept on follow-up. Postoperative radiographs at three months demonstrated a stable fibular graft with no evidence of local recurrence.

Case 4

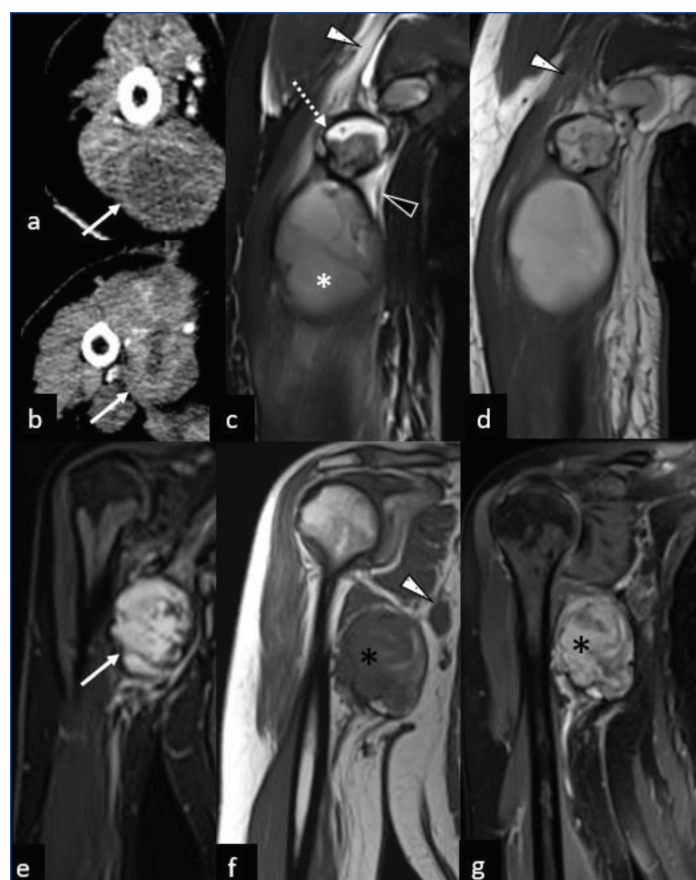
A 52-year-old farmer presented to the vascular surgery OPD with recurrent right axillary swelling and bleeding episodes over 15 months. He was evaluated elsewhere with an MRI, which was reported as a haematoma, and was transfused for the blood loss.

In view of recurrent symptoms, an angiomatous lesion was suspected, and a Fine Needle Aspiration Cytology (FNAC) was performed

elsewhere, which was reported as negative for malignant cells in a background of dense haemorrhage. Surgical exploration was subsequently performed at the same centre, and the postoperative biopsy was reported as an organising haematoma. Despite these interventions, the patient experienced persistent bleeding, requiring 10 blood transfusions along with fresh frozen plasma support.

At this point, he presented to our institute. Clinical examination revealed a fullness measuring approximately 10×15 cm in the right axilla and medial upper arm. The swelling was soft, non-fluctuant, with local warmth, and no pulsatility or bruit. The overlying skin was not fixed to the underlying lesion but was ulcerated with active serosanguinous discharge. The patient also had power of 4/5 in the right upper limb, with intact sensation, and distal pulses were palpable. Laboratory investigations showed severe anaemia (haemoglobin 4.6 g/dL), while the coagulation profile (APTT- 35 sec, PT/INR- 13/1.2, platelet count- 160,000) remained unremarkable.

Given the suspicion of an angiomatous lesion, a CT angiogram was performed, which demonstrated a 6×5×5.5 cm circumscribed, lobulated, rim-enhancing hypodense mass within the muscular planes of the axilla and upper arm [Table/Fig-4a]. The anterior and posterior circumflex humeral arteries were encased, and the right axillary artery and vein were abutted. No active contrast extravasation or features to suggest a pseudoaneurysm or vascular malformation were seen. MRI revealed multiple haemorrhagic collections without a definite solid component within the triceps, coracobrachialis, and axillary fat pad, encasing the distal brachial plexus and axillary vessels [Table/Fig-4c-g]. Given the inconclusive imaging findings, an excision biopsy of the arm component was performed, which was suggestive of AFH.



[Table/Fig-4]: A 52-year-old male presenting with right axillary swelling. Initial CT angiogram axial images: (a,b) demonstrate a circumscribed, lobulated, rim-enhancing hypodense lesion (arrows) within the muscular planes of the upper arm and axilla. MRI, including coronal STIR; (c) and coronal T1-weighted; (d) images, reveals multiple lobulated cystic lesions with T2-hypointense rims (dotted arrow), internal blood-fluid levels (asterisk), and mild perilesional oedema (black arrowhead) in the posteromedial right arm and axillary fat pad, encasing the distal brachial plexus and axillary vessels (white arrowhead). Follow-up MRI, including coronal STIR; (e), T1-weighted; (f), and postcontrast T1-weighted; (g) images, demonstrates interval increase in size of the axillary component (arrow), with development of an enhancing solid component (asterisk) and multiple enlarged axillary lymph nodes (arrowhead).

He was advised excision of the residual lesion; however, he was unwilling to proceed at the time due to personal constraints. He returned two months later with rapid interval growth and severe re-bleeding. The interventional radiology team planned and performed preoperative embolisation to reduce surgical risk. Tumour blush was noted arising from the posterior circumflex humeral artery, which was selectively cannulated and embolised with Polyvinyl Alcohol (PVA) particles. Intraoperative blood loss was minimal, with no significant intra- or postoperative complications. Repeat contrast-enhanced MRI was performed to assess the extent, revealing an enhancing solid component with further increase in lesion size and multiple enlarged axillary nodes [Table/Fig-4b].

He subsequently underwent excision of the residual lesion; however, an R0 resection was not achievable due to the extensive encasement of major neurovascular structures. Histopathological analysis confirmed AFH. Notably, the enlarged axillary lymph nodes were found to be reactive and tumour-free. Unfortunately, this patient was subsequently lost to further follow-up.

DISCUSSION

The AFH often presents as a soft-tissue mass in the subcutis or deep dermis in the extremities of children and young adults [2]. The present study findings differ from those reported by Saito K et al., who described seven cases with a male predominance (5/7), an age range of 8-50 years, and predominantly extremity involvement. In their series, four tumours were subcutaneous and three were located in deep tissues [2]. In contrast, all four tumours in the present series demonstrated deep involvement, with bone involvement in two cases and facial nerve involvement in one, indicating a more locally infiltrative pattern. While Saito K et al., reported predominantly painless masses, with only one patient presenting with pain, two of the patients presented with painful swelling. Fever and anaemia, which are uncommon clinical manifestations of AFH, were present in one of the cases [2].

Key MRI characteristics identified in the literature and in the present case series include [3]:

- **Fluid-fluid levels:** These are frequently observed and represent sedimented blood products within the tumour's characteristic "angiomatoid" cystic spaces. While also seen in Aneurysmal Bone Cysts (ABC) of soft-tissue and giant cell tumours, their presence in a superficial extremity mass Image consent declaration incomplete in a child is highly suggestive of AFH [4].
- **Fibrous pseudocapsule:** Often appearing as a hypointense rim on both T1 and T2-weighted images with prominent enhancement.
- **Susceptibility artefacts:** Foci of low signal intensity representing haemosiderin deposition.

Few recently described signs include:

- **The "double rim sign":** A high-signal outer rim and a low-signal inner rim on T2-weighted and postcontrast images reflects the peripheral lymphoid cuff and the internal fibrous pseudocapsule, respectively [5].

As illustrated in Case 4, when there was clinical suspicion of an angiomatous lesion, a postcontrast MRI was preferred over a non-contrast MRI, as haemorrhage may have variable appearance and mask the presence of an underlying solid lesion.

Definitive diagnosis rests on histopathological and Immunohistochemical (IHC) analysis. Microscopically, AFH is characterised by a multinodular growth of spindle cells, a prominent peripheral lymphofollicular infiltrate, and internal haemorrhagic spaces [2]. "Immunohistochemistry is supportive rather than diagnostic; approximately half of AFHs express desmin, while CD68 and CD99 show variable expression [6]. Molecular confirmation via EWSR1-ATF1 or EWSR1-CREB1 fusion detection offers a more specific diagnostic adjunct [7,8].

This case series is limited by its small sample of four patients, retrospective, single-institution design, heterogeneous imaging work-up, and the absence of a comparator group of imaging mimics.

CONCLUSION(S)

The AFH is a significant diagnostic mimic that must be considered in the differential diagnosis of cystic musculoskeletal masses. The presence of fluid-fluid levels, a T2-hypointense fibrous rim, and regional lymphadenopathy should prompt a suspicion of AFH.

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