Angiomatoid fibrous histiocytoma in an elderly male: An unusual presentation with review of literature

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Received – 07 September 2017 Initial Review – 27 September 2017 Published Online – 07 January 2017

ABSTRACT

Angiomatoid fibrous histiocytoma (AFH) is a rare soft tissue tumor occurring mostly in children, adolescents, and young adults. Clinically and radiographically, it is difficult to differentiate AFH from hematoma, soft tissue hemangioma, and malignant fibrous histiocytoma. Here, we present the clinical, radiologic, and pathologic findings of a case of AFH due to its rarity in a 67-year-old man. The patient underwent wide surgical excision with a provisional diagnosis of sarcoma. On pathological examination, the lesion demonstrated solid-cystic nodules of histiocytes with blood-filled cysts, a dense hyaline fibrous pseudo capsule, and a very focal peripheral lymphoplasmacytic infiltrates. The tumor cells showed strong positivity for CD68, variable positivity for CD34, Desmin, EMA, negativity for CK and a low Ki67 index.

Key words: *Cytokine, Sarcoma, Tumor*

Angiomatoid fibrous histiocytoma (AFH) is a rarely metastasizing soft tissue tumor of uncertain differentiation. It accounts for only about 0.3% of all soft tissue tumors [1,2]. Most of the patients present in the first 3 decades of life; however, cases occurring in wide age range have been reported. There is no significant sex predilection. It frequently occurs superficially in the deep dermis and subcutis of the extremities as a slowly growing, superficial nodular mass [3]. Some patients experience systemic symptoms such as pyrexia, anemia, and malaise due to tumoral cytokine production [4]. Clinically and radiographically, the lesion is easily confused with a hematoma, soft tissue hemangioma, or malignant fibrous histiocytoma. Making a pre-operative diagnosis of AFH is challenging with no distinct clinical or imaging findings to lead to a diagnosis. Correct diagnosis is important because of the small risk of metastasis and death.

When Enzinger initially described "angiomatoid malignant fibrous histiocytoma" in 1979, 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. The 2002 World Health Organization classification removed it from the malignant fibrous histiocytoma subtype of sarcoma (now synonymous with undifferentiated pleomorphic sarcoma) and classified it as tumors of uncertain differentiation as AFH [5]. Here, we present a case report of this rare tumor in unusual age group (elderly male) which had a provisional clinico-radiological diagnosis of sarcoma. Moreover, very focal lymphoplasmacytic inflammatory infiltrate made diagnosis a challenge in the present case.

CASE REPORT

A 67-year-old male presented with a left thigh swelling for past the 3 years which was gradually increasing in size. Swelling was painless to start with, but the patient developed dull aching, continuous pain for the past 1 year. There were no complaints of fever, malaise, or weight loss. On examination, there was a 20×16 cm soft, fluctuating, mildly tender swelling over lateral compartment of left thigh. Laboratory studies revealed anemia with hemoglobin of 10.3 g/dL (reference 13.5–17.5 g/dL). His erythrocyte sedimentation rate was 45 mm in 1 h (normal 0–22 mm in 1 hour). Magnetic resonance imaging (MRI) revealed a 19.9×14×11 cm mixed solid cystic multiloculated, heterogeneously enhancing mass with internal hemorrhage in the subcutaneous left lateral proximal thigh. No evidence of underlying muscle invasion was evident. Clinico-radiological diagnosis of sarcoma was made.

Repeated Fine needle aspiration attempts revealed degenerated cells alongwith a blood mixed mucoid material and no presumptive diagnosis could be made. Punch biopsy revealed only adipose and fibrocollagenous tissue and further led to diagnostic dilemma. Surgical excision of the entire tumor alongwith involved fascia lata was done with a provisional clinico-radiological diagnosis of sarcoma. Tumor was 10×9×6 cm in size, solid-cystic, firm, lobulated, multinodular with myxoid, necrotic, and hemorrhagic areas (Fig. 1a). Cystic areas were filled with blood. Periphery of the tumor was gray-white firm. Overlying skin was thinned out. Microscopic examination revealed variably sized blood-filled cystic spaces surrounded by sheets of histiocytes with bland,

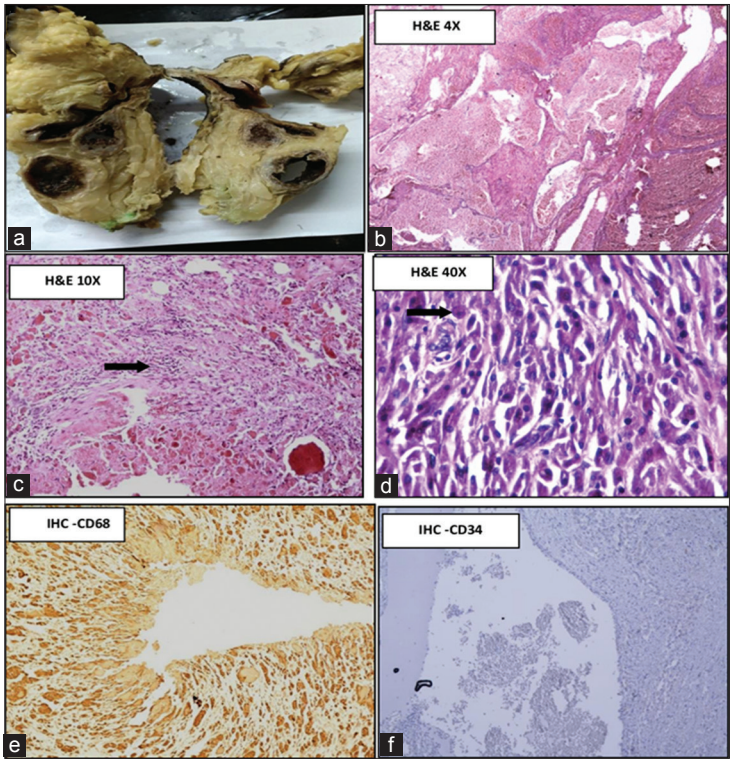

Figure 1: (a) Gross finding-showing solid cystic cut surface with blood filled cystic space, (b) H and E 4× - Showing many blood-filled pseudo vascular channels, (c) H and E 10× - Showing very focal lymphocytic inflammatory infiltrate (black arrow), (d) H and E 40× - Showing spindle shaped cells along with hemosiderin-laden macrophages (black arrow), (e) immunohistochemistry (IHC) - CD68 positive histiocytes surrounding pseudo vascular spaces, (f) IHC - CD 34 negativity in cells lining pseudo vascular spaces

vesicular nuclei with few showing mild nuclear atypia along with hemosiderin-laden macrophages and giant cells (Fig. 1b and c). Few spindle-shaped cells and occasional cells with more abundant cytoplasm (rhabdomyoblast like cells) (Fig. 1d). However, no striations were seen and thus initial provisional diagnosis of rhabdomyosarcoma was excluded. Surrounding these blood-filled cystic spaces was a fibrous pseudocapsule. We did not get much lymphoplasmacytic infiltrate initially. Only after extensive sectioning, focal area of lymphoplasmacytic infiltrate was found (Fig. 1c). Areas of necrosis and calcification were also seen. Immunohistochemistry (IHC) showed strong positivity for CD68 in the histiocytes lining the pseudo vascular spaces, variable positivity for CD34 (Fig. 1f), desmin, epithelial membrane antigen (EMA), negativity for cytokeratin, and low Ki67 index of 2% (Fig. 1d and e). Diagnosis of AFH was made based on histopathology and immunohistochemistry.

DISCUSSION

AFH was first described in 1979 [6]. It typically occurs in the extremities of children and young adults as a slowly growing, superficial nodular mass; although wide age range has also been reported [7]. AFH in elderly is very rare with very few cases reports could be found after an extensive review of literature. The majority of cases occur in the extremities; although cases have been reported in the head and neck region (10%) and trunk. The tumor is rare, accounting for approximately 0.3% of all soft tissue neoplasms. It is likely to have been previously underdiagnosed and placed under other neoplastic categories (vascular, fibrohistiocytic, and myofibroblastic types).

Making a pre-operative diagnosis of AFH is difficult. Imaging studies alone cannot differentiate AFH from sarcoma. Although nonspecific, a mass with MRI findings of cystic areas, enhancing fibrous pseudo capsule, and internal areas of hemorrhage in the extremity of a child or adolescent should prompt the differential of AFH. However, some cases may show predominantly solid areas. Wide surgical excision and post-excisional monitoring are essential.

The diagnosis of AFH is based on histopathology and IHC. Macroscopically, AFH is generally firm and circumscribed. The characteristic microscopic appearance includes a fibrous pseudo capsule, pseudoangiomatous cystic spaces surrounded by round to spindle fibrohistiocytic cells with bland, vesicular nuclei, and a plasma lymphocytic infiltrate [7,8]. IHC shows variable positivity for desmin, CD68, and CD99 [9].

The differential diagnosis of AFH is wide-ranging from benign granulomas to malignant neoplasms. AFH of long duration can mimic hematoma due to extensive fibrosis, hemorrhage, and hemosiderin deposition. Granulomatous inflammation can be differentiated due to lack of vascular spaces in them and more solid appearance of AFH. Spindle cell hemangioma is poorly circumscribed with true vascular spaces as compared to fairly circumscribed pseudoangiomatous lesion, AFH. Nodular Kaposi sarcoma presents as a circumscribed dermal lesion with bland cytology containing slit like blood-filled spaces unlike the blood-filled cysts are seen in AFH. Rhabdomyosarcoma is situated

deeply and is infiltrative without a peripheral lymphoid cuff when compared with AFHs.

About 80% cases of AFH show dense lymphoplasmacytic infiltrate, unlike our case which showed only focal infiltrate after extensive sampling. Thus, the only constant finding of AFH is the presence of sheets of oval to spindled cells, and features such as fibrous capsule or lymphoplasmacytic infiltrate may be absent or not sampled [8].

As AFH lacks a specific immunophenotypic, IHC is supportive and not diagnostic. There is variable immunoreactivity for the EMA, desmin, CD68, smooth muscle actin, calponin, and CD99 [9]. Molecular studies are most helpful for confirming a diagnosis of angiomatoid fibrous histiocytoma but was not available in our case. Distinctive chromosomal translocations are found angiomatoid fibrous histiocytoma, with *EWS/CREB1*(CAMP responsive element binding protein 1) fusion being the most common (>75% of cases), others being *EWS/ATF1* and *FUS/ATF*.

Most AFHs have a benign course with local recurrence seen in up to 15% of cases and <5% cases showing metastasis, predominantly to regional lymph nodes followed by lungs, liver, or brain [6]. However, deaths from distant metastases have rarely occurred. Appropriate management is wide local excision with follow-up as it has a small risk of metastasis and death. Adjuvant radiotherapy or chemotherapy may be required in unrespectable cases and those showing metastasis. Our case has been followed up and found to be disease-free after 10 months of surgery. No chemo or radiotherapy was given to the patient.

CONCLUSIONS

AFH is a rare disease that is often misdiagnosed initially due to its wide variation in morphology, site of occurrence and bland morphology. AFH can recur locally, but most of these patients do well with wide local excisions alone. Histopathology and IHC findings point toward diagnosis of AFH, however, molecular studies can only lead to confirmation. Correct diagnosis and close clinical follow-up of AFH patient is important as it has a small risk of metastasis and death.

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Funding: None; Conflict of Interest: None Stated.

How to cite this article: Pahuja S, Kashyap A, Agarwal K. Angiomatoid fibrous histiocytoma in an elderly male: An unusual presentation with review of literature. Indian J Case Reports. 2018;4(1):35-37.