Angiomatoid Fibrous Histiocytoma: A Rare Cause of Anemia in a Child

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Abstract

Angiomatoid fibrous histiocytoma (AFH) is a rare soft tissue tumor of intermediate potential and is usually found during first two decades of life. It is located mainly in extremities presents as a painless, slow growing mass with extensive blood supply. Embryologically, it arises from a pluripotent mesenchymal cell. Histologically, the tumor has thick pseudo capsule with chronic inflammatory infiltrates and hemorrhagic cystic areas. We present a case of AFH which caused severe anemia in a child with a non-healing ulcer on the medial aspect of left knee. Multiple blood transfusions, incision and drainage and biopsies were done however; only complete surgical resection proved to be fruitful. The biopsy is EMA positive, cytokeratin AE1/AE3 & Desmin are focal positive. CD21 highlights meshwork of follicular dendritic cells. Yearly follow up is advised. Angiomatoid Fibrous Histiocytoma should be kept in the differentials while managing hematoma-like lesions in the extremities. It is often misdiagnosed thus prompt treatment is usually delayed. The prognosis after complete surgical resection is good but chemotherapy should be considered in recurrent cases.

Key words: Angiomatoid fibrous histiocytoma, AFH, soft tissue tumor, children, Anemia

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Introduction

Angiomatoid fibrous histiocytoma (AFH) was first described in 1979 by Enzinger, as a malignant form and then was changed to a tumor of intermediate potential. Histologically tumor is seen as a thick pseudo capsule with chronic inflammatory infiltrates and hemorrhagic cystic areas. In 2002, the World health organization (WHO) removed AFH from the malignant fibrous histiocytoma subtype of sarcoma and changed it to the category of tumors of uncertain differentiation as AFH.[1]

Angiomatoid fibrous histiocytoma is a rare, low grade, soft tissue tumor more common in young, usually a slow growing tumor and it rarely metastasizes.[2] Most of the time, it appears as a painless soft tissue mass in the subcutaneous or deep dermal layers of the body.[3]

Clinically and radiologically the tumor can be confused with hematoma or soft tissue hemangioma.[1] It is a unique borderline neoplasm with inert behavior, predominantly arising in the superficial tissues in the extremities.[4] It presents as a mass in subcutaneous region in extremities. The prognosis is generally good, the rate of recurrence is about 15% and the rate of metastasis is less than 1%.[5] Symptoms include anemia, weight loss, fever; pain or tenderness are extremely rare. Embryologically, AFH arises from a pluripotent mesenchymal cell because morphologically it shows vascular, histiocytic, smooth, and striated muscle differentiation. Microscopically, AFH shows solid arrays or nests of histiocyte-like cells, hemorrhagic cyst-like spaces, and aggregates of chronic inflammatory cells. Multifocal recent and old hemorrhages and inflammatory cells are distinctive feature of this tumor. A thick pseudo capsule with germinal centers makes it resemble with a lymph node.[1] Most common treatment option is wide surgical excision and has proven to keep the patient disease free in most of the cases.[5] Chemotherapy has shown significant results in the recurrent cases of AFH.[9]

This case report will present a rare cause of severe anemia

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due to AFH and its various clinical, radiological and histopathological findings along with the definitive treatment that was provided for AFH.

Case

A 4-year-old male presented to Shaikh Zayed Medical Complex, Lahore in January 2021 through outpatient department with complaint of a non-healing wound on medial side of left knee that was oozing blood for last 4 months. The child was previously taken to a tertiary care hospital in Lahore where incision & drainage was done but the operative findings were not available. After that the patient developed a non- healing wound. Patient was taken to different hospitals and biopsy was taken, that showed a benign ulcer with granulation tissue.

In the meantime, patient continued to ooze blood from the affected area and developed severe anemia for which he received blood transfusion three times over 4 months. Hematologist was consulted as well and the patient was investigated extensively for bleeding disorders but no bleeding disorder was found. There was no history of bleeding disorder in family or patient. No history of weight loss, anorexia or fever. Rest of the history was unremarkable.

On physical examination there was marked pallor, small mobile, left sided inguinal lymph nodes were palpable. Local examination showed a profusely bleeding ulcer about 5×5cm, oval shaped with irregular margins and a granulation tissue pouting out of the floor of ulcer, that bled on touch. (Fig.1)

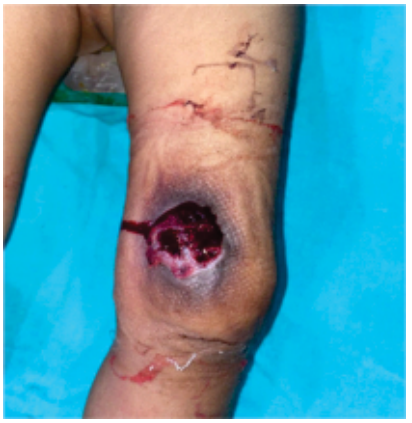

Fig 1: *Ulcer at the Time of Presentation*

Investigations done at the time of admission showed Hemoglobin level of 4g/dl. Bleeding factors, clotting time, bleeding time and rest of the baseline tests were within normal range. Arteriovenous Doppler ultrasound of left leg pointed out a large superficial bleeding wound on medial aspect of left knee joint with underlying cellulitis and mild joint effusion measuring 2.2*1.2*2.5 cm, approximate 34ml. Multiple large left sided inguinal lymph nodes were also mentioned. Short axis diameter was 1cm and showed some necrosis. Rest of the ultrasound was normal.

Excision of the tissue was done under general anesthesia. The lesion was extending up to deep fascia but was superficial to muscles with tendency to bleed. The sample was sent for histopathology. (Fig. 2)

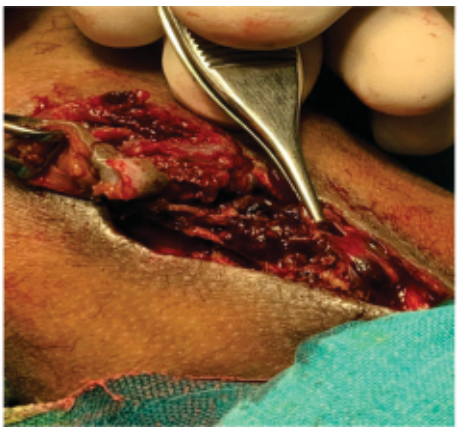

Fig 2: *Wound at the time of first debridement containing vascular tissue.*

The biopsy showed benign ulcer with granulation tissue.

On follow up after 15 days, patient had superficial wound infection. However, there was no history of bleeding and he did not require blood transfusion. The wound was cleaned. (Fig. 3)

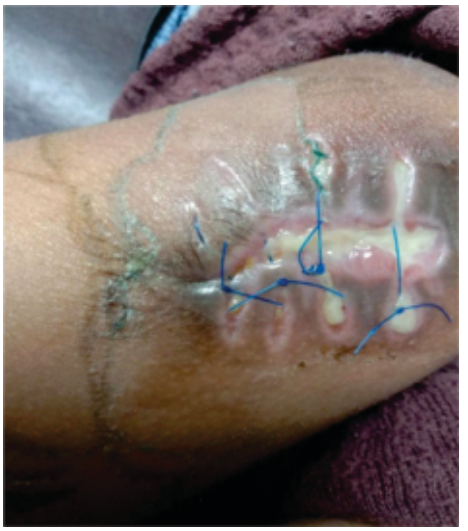

Fig 3: *Infected wound on follow up*

A soft inguinal swelling was noted on left side after

about 22 days of initial resection. On examination the swelling was 2*2cm, non-tender, non-erythematous with overlying skin discoloration. Ultrasound of inguinal swelling revealed enlarged lymph node with increased vascularity. Patient was admitted again for excisional biopsy of inguinal swelling. (Image. 4)

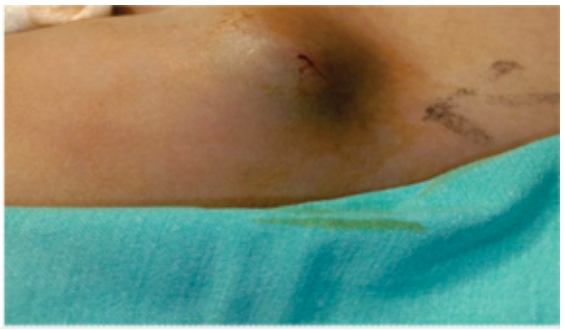

Fig 4: *Inguinal swelling*

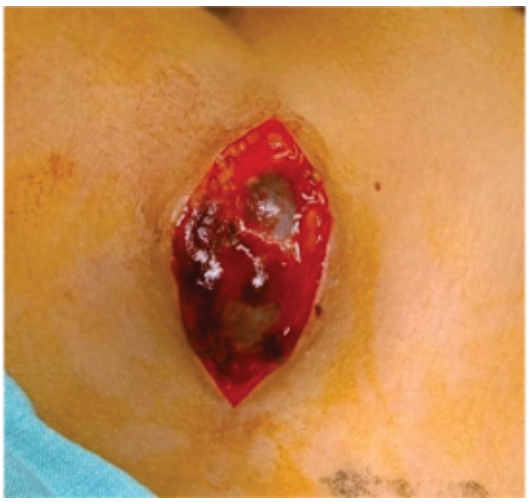

Fig 5: *Intraoperative image showing inguinal swelling*

The inguinal swelling was aspirated before excision and frank blood was drained. Intraoperative findings showed highly vascularized lymph nodes with surrounding vessels. Lymph node was completely excised. Sample was sent for histopathology. EMA, cytokeratin AE1/AE3, Desmin, ASMA, CD34, Myogenin, SALL-4, CD21 stains were done on the specimen. EMA was positive, cytokeratin AE1/AE3 & Desmin were focal positive. CD21 highlighted meshwork of follicular dendritic cells. The final histopathological diagnosis was Angiomatoid fibrous histiocytoma. On three months follow-up the patient was in good health, inguinal swelling had disappeared, primary wound had healed, no blood transfusion was required. Patient was referred for the opinion of the oncologist who advised regular folowup only.

Discussion

This case report demonstrates a very rare cause of soft tissue mass in the pediatric age group. AFH can easily be confused with hematoma, hemangioma, lipoma, leiomyosarcoma. AFH is a low grade and usually a slow growing tumor, more common in extremities with a good prognosis. AFH is composed of blood or fluid filled cystic spaces.[1] The pathological examination of the lesion may also be confused with metastatic carcinoma or melanoma, regardless of the presence of peculiar morphology.[6] Our case presented with severe repeated anemia due to the blood loss from the lesion and patient also required multiple blood transfusions.

A study carried out in 2011, showed that the rate of recurrence is about 15% and the rate of metastasis is about 1%.[7] In our case the disease involved local inguinal lymph nodes and after complete surgical resection of the primary as well as the inguinal swelling no other lesion was noted. According to a study conducted in 1991, immunohistochemistry demonstrates AFH to be positive for CD 68 and desmin.8 However, recent cytogenic studies have shown WSR1-CREB1 fusion gene reported in many cases.5 In our case, EMA was positive, cyto-keratin AE1/AE3 & Desmin were focal positive. CD21 highlighted meshwork of follicular dendritic cells.

Surgical resection proves to be beneficial in majority of the cases.[1] Most of the studies have shown wide surgical excision as a definitive treatment and patients remained disease free in most of the cases[5]. Our case report demonstrates complete surgical resection alone to be fruitful without chemotherapy and the child was asymptomatic thereafter.

Chemotherapy is not mainly used for the initial disease but has shown significant results in the recurrent cases of AFH along with regional lymph node metastases that occurred after wide local excision of primary lesion.[9]

According to a case reported in 2018 at Texas Children's Cancer Center, Tocilizumab which is an IL-6 receptor inhibitor antibody has shown good response in a child with treatment-refractory metastatic AFH with EWSR1-CREB1 fusion and elevated serum IL-6 as compared to the other chemotherapeutic agents. The disease reappeared after discontinuing tocilizumab for one year. Tocilizumab is generally well tolerated and is a suitable alternative for recurrent or metastatic AFH in comparison

to the conventional chemotherapeutic agents.[10]

A case series of seven cases compiled in Japan reports two out of the total cases to metastasize to distant sites, one of whom died due to these complications.[11] Literature shows AFH to recur in 15% of patients,[12] but metastasize in only less than 1%.[13] Very few of AFH lesions are primarily diagnosed as AFH even after complex imaging such as Magnetic Resonance Imaging (MRI) which shows homogenous hypointense lesions on T1 and hyperintense heterogenous lesions on T2.14 Although some studies have shown a 'double-rim' sign as a classical finding of AFH on MRI.[15] this has not been backed up by other case reports which claimed it to be present just due to the pseudocapsule and the subsequent peritubular edema. Costa et al reported local recurrence being associated with the irregularities in the border of the tumor and metastasis being in direct relation with the depth of the tumor.[15] Morgan et al reported a secondary paraneoplastic platelet function disorder that resulted in bleeding and intractable anemia.[16]

Substantial number of cases have been reported and research work has been done internationally but limited data is available in Pakistan. According to recent literature, the best diagnostic indicator for AFH is the presence of lymphoplasmacytic infiltrate around the tumor,[17] a feature rarely present in other tumors. Although it is also present in gastrointestinal shwannomma.[18] In addition, the location of these tumors is diverse, including but not limited to soft tissues, brain, lung, mediastinum, omentum and bone but most commonly occurring in the deep dermal or the subcuticular layer of extremities in the younger population.[19] It is expected that more locations will be added in the future owing to its diverse immunohistochemistry and pathophysiology. Furthermore, Chen at al from China indicates a high degree of probability of it being misdiagnosed as myofibroblastic tumors, dendritic cell sarcoma or poorly differentiated meningioma.[20] Hence, AFH has a morphological spectrum ranging from granulomas to both benign and malignant neoplasms.[21] extensive research is required to properly define the diagnostic criteria to aid in its better recognition and management.

This case represents the clinical, hematological, radiological and histopathological features of AFH. AFH often tends to be misdiagnosed so inadequate treatment can be provided sometimes by the physicians but the surgeons should keep this tumor in mind while treating any such mass. This case presented as a non-healing wound which bled profusely leading towards severe anemia. The incidental diagnosis made it clear that even the minor non healing wounds should not be taken lightly. As this tumor is of intermediate potential, therefore, yearly follow up and radiological surveillance is advised.

Conclusion

This case study shows that even the minor non healing wounds should not be taken lightly and unusual causes should always be kept in mind when treating such cases and anemia without any apparent medical cause should be extensively investigated.

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Authors Contribution

AI: Conceptualization of Project
AI: Data Collection
MZK: Literature Search
: Statistical Analysis
MAS: Drafting, Revision
JG: Writing of Manuscript