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Myxoid Type of Malignant Fibrous Histiocytoma (myxofibrosarcoma) - A Case Report of an Unexpected Histopathology of Intermuscular Mass

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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Case Report

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ABSTRACT

Malignant fibrous histiocytoma is a rare and highly aggressive neoplasm believed to originate from primitive mesenchymal cells; arising from soft tissue or bone, usually in the extremities (large muscles of thigh) or retroperitoneum. It is now referred to as undifferentiated pleomorphic sarcoma (UPS). This neoplasm is the most common soft tissue sarcoma of late adult life and has a slight male predominance. The mostcommon is storiform/pleomorphic that forms 50-60% of all such tumours while myxoid type is the second most common at 25%. A 57-year-old male presented to us with a swelling over the antero-lateral aspect of upper and middle third of left thigh measuring about 20 x 15 centimeters. He was thoroughly investigated and swelling was excised in toto. Soft swelling excised and on histopathology found to be an intermuscular myxoid type of malignant fibrous histiocytoma (high grade myxofibrosarcoma). Excisions of intermuscular lesions is not an uncommon story but most are confirmed to be benign myxomas or nerve sheath cell tumor. However, the entity of malignant fibrous histiocytoma should be kept in mind. Patients will usually present late with advanced local disease or metastasis, usually to lungs and lymph nodes. Treatment is surgical with wide local excision and neoadjuvant/adjuvant radiotherapy has been advocated as well. This case report is being presented as the tumor is rare and also an important

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consideration in the differential diagnosis of myxomas, intermuscular lipomas, peripheral nerve sheath tumor, hemangioma, hematoma and desmoid tumor. Another important feature is that the tumor can be diagnosed with certainty only after excision with histopathological examination.

Keywords: Myxoid; malignant fibrous histiocytoma; histopathology; intermuscular mass.

1. INTRODUCTION

Malignant fibrous histiocytoma (MFH), a type of sarcoma, is rare and malignant neoplasm of uncertain origin believed to originate from primitive mesenchymal cells that arises both in soft tissue and bone usually from extremities [1]. In 2002, WHO declassified MFH as a formal diagnostic entity and renamed it as an undifferentiated pleomorphic sarcoma not otherwise specified is classified under the undifferentiated/unclassified sarcomas group [2]. This new terminology has been supported by an evidence to suggest that MFH represents final common pathway in tumors that undergo progression towards undifferentiation. While it remains unclear how to most accurately organize these tumors.

This neoplasm is the most common soft tissue sarcoma of late adult life (approximately 50 to 70 years of age) [3] and has a slight male predominance. It has been categorized into five subtypes: storiform/pleomorphic, myxoid, giant cell, inflammatory, angiomatoid. The most common is storiform/pleomorphic that forms 50–60% of all such tumours while myxoid type is the second most common at 25% [4]. About 20% of all sarcomas are the undifferentiated/unclassified type and about a quarter of those are radiation related [5]. Patients usually present late with metastasis, most frequently to lungs or lymph nodes [6,7]. Imaging like Computed Tomography (CT) or Magnetic Resonance Imaging (MRI) scans play a role in defining the extent of the disease and the treatment is mainly surgical. There may be a role for neoadjuvant/adjuvant radiotherapy [8]. Unlike the other subtypes of MFH, the myxoid form tends to be less aggressive and as a result is associated with a better prognosis. The myxoid subtype must contain at least 50% myxoid areas by definition. Occasionally an entire nodule of tumor can have a myxoid appearance causing diagnostic confusion including less aggressive entities such as myxoma or nodular fasciitis. Most myxoid variants of MFH behave as low-grade neoplasms and thus pursue a less aggressive course. Soft tissue MFH can arise in any part of the body but most commonly in the lower extremity, especially the thigh and retroperitoneum. Patients often complain of a mass or lump that has arisen over a short period of time ranging from weeks to months. It is common for patients to report trauma to the affected area. Trauma as far as we know does not cause MFH but rather the incident draws attention to the extremity. Mass does not cause any pain unless it is compressing a nearby nerve. Despite the tumor having encapsulated look on gross examination with well-defined borders, the lesion microscopically infiltrates the muscle and fascial planes. The vast majority of metastatic disease from sarcomas including MFH present as pulmonary disease (90%). Involvement of extra pulmonary sites is uncommon: lymph nodes (10%), bone (8%). Liver (1%) [9].

2. CASE REPORT

A 57-year-old male patient presented to us with swelling of the left thigh which was noticed following trauma since 1 week. The swelling was painless and had gradually increased in size prior to presentation to us. The swelling over antero-lateral aspect of upper and middle one third of left thigh measured about 20 x 15 centimeters, soft in consistency, non-mobile, non-tender, no lymphadenopathy appreciated on examination and prominence on active muscle contraction (Fig. 1 A, B). He had not had similar lesion on any other part of his body before. Medical history included hypertension on medication (Telmisartan 40 mg OD). No significant surgical history.

The patient was investigated with MRI which revealed a large well defined oval shaped thin-walled capsulated cystic appearing lesion measuring 20.5 (CC) X 10.6 (TR) X 9.0 (AP) cm in size, located in an inter-muscular location in antero-lateral compartment of left thigh. The lesion is located deep to the rectus femoris and vastus lateralis causing its splaying and superficial to vastus intermedius muscle with a mildly iso to hypointense enhancing eccentric mural nodule (2.4 x 1.9 cm) present in the superior part of the lesion and intralesional abnormal signal intensity suggestive of myxomatous lesion. (Fig. 2 A, B).

FNAC revealed paucicellular smears showing few scattered spindle cells, small clusters of adipocytes, thin capillaries and focal myxoid material over a hemorrhagic background. Routine blood examination had not revealed any abnormality. All of these investigations were performed before the patient sought treatment at our institution.

On operation the lesion was discovered to be deep, extending down to the fascia clearly demarcated not involving muscle and extensively vascular. One piece measuring 20 cm x 10 cm x 3 cm was removed in entirely with two tumour nodules adjacent to it looking like lymph node with adequate margins under spinal anaesthesia (Fig.3 A). It was well encapsulated mass. Patient had no post-operative complications and was discharged after four days with negative pressure suction drain in situ at operated site which was removed on post-op day eight.

The gross pathological examination revealed A single globular soft tissue mass measuring (19x 13x 4.5) cm and weighing 930 grams. Outer surface was grayish brown, bosselated and showed prominent vascular marking. On serial sectioning cut surface was soft grayish white, jelly like with congestion at places. There was a firm area measuring (3.5x 2.5x 1.5) cm cut surface of which is grayish brown and solid. There was a nodule over the surface measuring (3x 2.2x 1.3) cm cut surface of which was firm and whitish. There was an attached fibro fatty tissue with a nodule measuring (3.5x 2x 2) cm (Fig.3 B).

Microscopy showed an encapsulated tumor comprised of spindle shaped cells showing moderate nuclear pleomorphism, hyper-chromatism with variable mitotic figure ranging from 5/HPF to 17/HPF. There was variable cellularity ranging from large myxoid areas to very cellular areas showing spindle shaped cells arranged in fascicles and storiform pattern. In the cellular area, few tumor giant cells along with increased mitosis ranging from 15-17/10 HPF seen. The intervening area between the tumor cells showed very fine plexiform vasculature. Microsections from the separate nodule showed similar tumor tissue with areas of hyalinization. The tumor was abutting skeletal muscle bundles. No lymph node structure was identified in the nodule. Alcian blue: strongly positive, Reticulin: positive.

IHC: VIMENTIN-Strongly and diffusely positive, SMA-Focally positive, CD34-Focally positive, CD68-Positive (Fig. 4 A, B, C, D).

The histology showed it to be a myxoid type of malignant fibrous histiocytoma (high grade myxofibrosarcoma). Follow up was 2 weeks post procedure in OPD with wound healing well. He had undergone whole body PET CT scan shows mild focal subcutaneous and intermuscular fat stranding in the anterior aspect of left thigh, likely related to post surgical inflammation. Referral to oncologist was made for follow up and the patient is under observation with following up for any signs of recurrence or the presence of similar swellings at different locations.

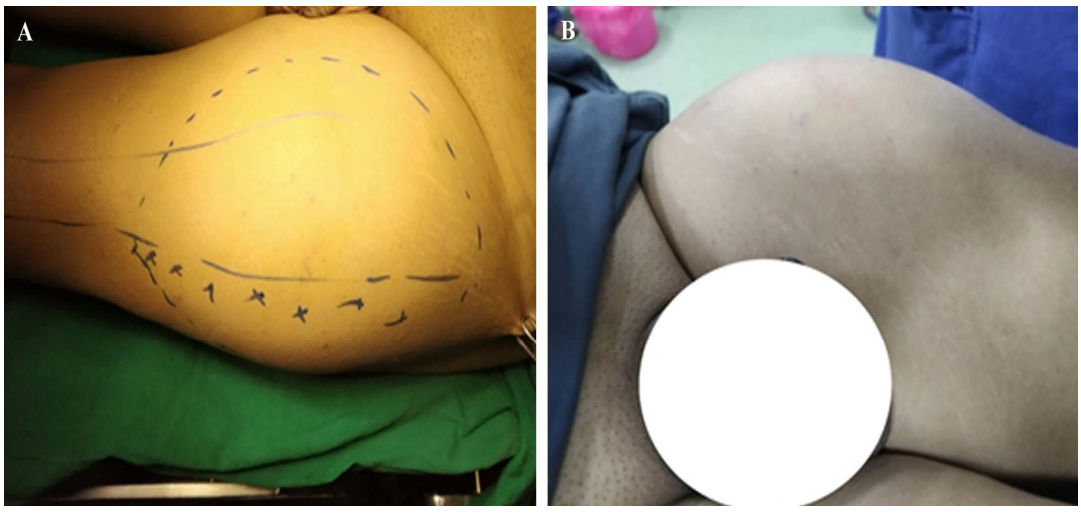

Fig. 1. A: Clinical photograph showing swelling in left upper and midthigh, B: Clinical photograph showing prominence of swelling on active muscle contraction

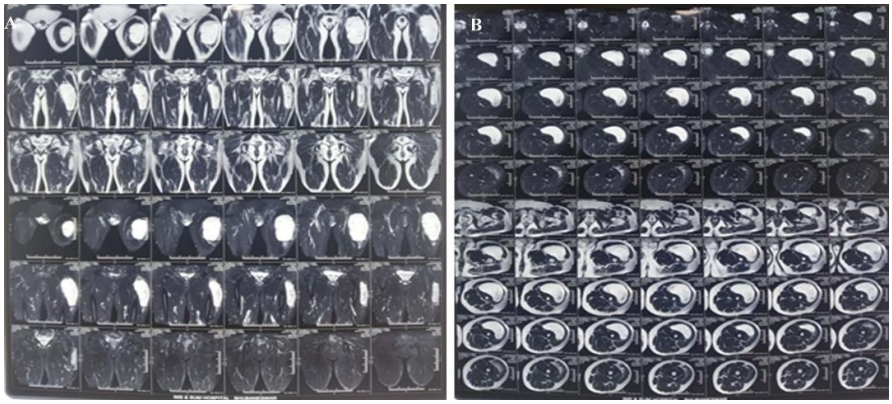

Fig. 2. A: MRI scan showing the lesion in sagittal plane, B: Axial section of lesion in T1 weighted image showing inter-muscular location

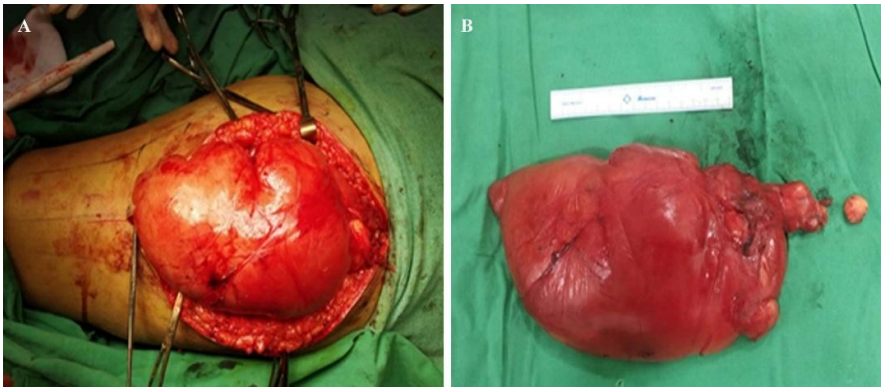

Fig. 3. A: Intra-operative picture showing clearly demarcated margins, B: Macroscopic picture of the lesion showing bosselated surface (Scale bar size: 15 cm)

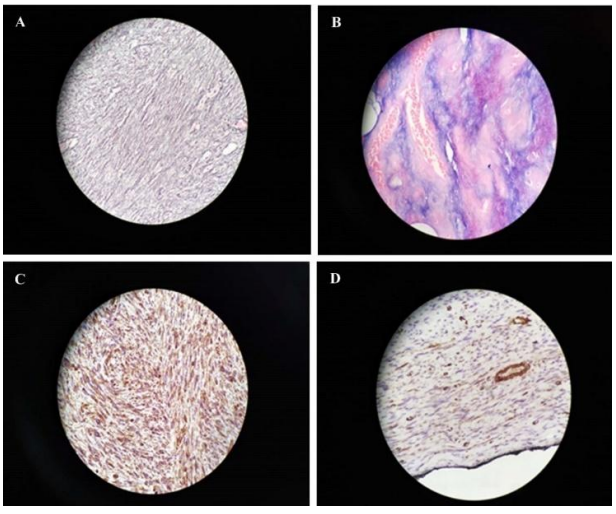

Fig. 4. A: Reticulin stain showing reticulin fibrosis, B: ALCIAN BLUE STAIN strongly positive for tumor, C: Vimentin (Strongly & Diffusely positive), D: SMA-Smooth Muscle Actin (Focally Positive)

3. DISCUSSION

Malignant fibrous histiocytoma, now referred to as undifferentiated pleomorphic sarcoma (UPS), is the most common soft tissue sarcoma of late adult life [6]. It was first introduced in 1961 by Kauffman and stout, they described MFH as a tumor rich in histocytes with storiform growth pattern. Despite the frequency of diagnosis, MFH has remained an enigma [9]. UPS can occur throughout the body with cases of visceral involvement being published [10,11]. Patients are usually between 32-80 years old with a slight male predominance. Our patient's histology showed the storiform/pleomorphic subtype that forms 50-60% of all such tumours while myxoid type is the second most common at 25% [4]. The other forms are rarer. Interestingly the inflammatory subtype mainly occurs in the retroperitoneum [5]. Symptoms are usually a painless, enlarging palpable mass [4], like the case with our patient. Local mass effect symptoms may because depending on location. Risk factors can include radiation treatment for another malignancy like Hodgkin's lymphoma [12], background history of Paget's disease, non ossifying fibroma and fibrous dysplasia. Soft tissue sarcoma has been linked to certain syndromes such as FAP and Gardner's syndrome, Li Fraumeni syndrome, Carney-Stratakis syndrome, Hereditary retinoblastoma, neurofibromatosis, BRCA2 gene mutations, [13,14]. In this case, the major contributing factor to developing UPS was most probably idiopathic not yet confirmed.

The diagnosis at histology involves microscopy, molecular studies and immunohistochemistry techniques. It is necessary for pathologists to have a consensus in classifying, grading and staging neoplasms and the World Health Organization Classification of Tumors of Soft Tissue and Bone facilitates that [2]. Our patient's tissue showed a myxoid characteristic and was given a GRADE 2/3. The cells showed significant pleomorphism with hyperchromatism, a mitotic count of 5-17/10 HPFs and less than 50% area of necrosis were seen. Immunohistochemical stains were done and the tumour was positive for Vimetin, smooth muscle actin (SMA), CD34 and CD 68 (Fig. 4). The tumour might have melanocytic markers (HMB-45, mel A), neural markers (S100), desmin, Bcl-2 (not shown). Further molecular studies include checking for BRAF mutations as the presence of BRAF mutation in these tumours raises the possibility that poorly differentiated spindle cell malignancies with BRAF mutation may represent melanomas [15]. BRAF is a gene that codes for B-Raf, a proto oncogene that is mutated in many human cancers. Another commonly mutated gene is p16. These mutations, if present, are not limited to malignant fibrous histiocytoma and this type of testing is not routinely done at our laboratory facility.

Imaging has a role with radiographs of the extremity (usual primary site) and chest (usual metastasis) being the first investigation done. MRI is the most useful test to image soft tissue tumors as it provides very valuable information about the mass such as size, location, and proximity to neurovascular structures. It is important to note that the diagnosis of a cancerous tumor cannot be made by MRI alone and Staging can be done once biopsy and imaging is completed by using the American Joint Committee on Cancer Staging Manual, 8th edition [16] (AJCCM).

These guidelines group soft tissue sarcomas by anatomical site and the histologic subtype, grade and tumor size which are essential for staging. TNM categories i.e., tumor size and extent, nodal involvement and distant metastasis are used. Histologic grade is based on the degree of differentiation, mitotic activity and extent of necrosis and helps determine risk better than the primary tumor size [16]. The grading scale used by The French Federation of Cancer Centers Sarcoma Group (FNCLCC) is preferred for its ease of reproducibility and ranges from Gx (cannot be assessed or graded) to Grade3 (total differentiation, mitotic score and necrosis score is 6, 7 or 8) [16]. Staging is then done using TNM and grading together to range from Stage 1 to Stage 4. *Staging for our patient was thus calculated to Stage IIIB (T4-tumor size >15 cm in greatest dimension + N0 + M0 + Grade 2/3).* T4 N0 M0 with G2/3 which is STAGE IIIB as per AJCC 8TH EDITION (staging systems for soft tissue sarcoma of the extremity or trunk).

Vanderbilt staging system: stage IIIB*(T3b-tumor >10 cm in greatest dimension, deep + N0 + M0 + G2/3)*

Prognosis varies and factors include size, grade, location and inflammatory component. Unfortunately most cases are found late at Stage 3 and 4, possibly with metastases but in our case no distant metastasis found as PET CT scan was done. They are aggressive and recur locally [17], which is not occurred in our patient. In a study done by Kearney et al. [18], a local recurrence

rate of 51% was seen in patients with a 'complete excision'. Pezzi et al. [7] found that the primary tumor size indicated the 5-year survival rate: tumors <5 cm had a survival rate of 82%; 5-10 cm, 68%; and >10 cm, 51%. The intermediate grade tumors showed a 5-year survival rate of 80%, and the 5-year survival rate for high-grade tumors was 60%. Survival rates for both grades were affected by size: tumors of high grade and smaller than 5 cm in diameter h ad a survival rate of 79%; 5–10 cm, 63%; and more than 10 cm, 41%. Superficial and distal located tumors were better. The size, depth and inflammatory component were important in metastasis; small sized, superficially located or with a prominently inflammatory component metastasized less frequently than large, deeper sited tumors [6,19]. The same staging system is used for the recurrence of lesion indicated with prefix 'r'. It must be kept in mind that the prognosis for the UPS in this case to be assessed with other factors. The main treatment of UPS remains complete surgical excision, with margins of at least 2 cm with a role for neo-adjuvant/adjuvant radiotherapy and doxorubicin-based chemo-therapy.

4. CONCLUSION

Malignant fibrous histiocytoma (myxofibro-sarcoma)/Undifferentiated pleomorphic sarcoma is a relatively rare malignant lesion affecting musculoskeletal system and should be a differential of a deeper lying lesion over extremities and trunk. It frequently presents in an advanced stage in older patients. Past history of any risk factors are significant. Surgical Local wide resection is advocated with a role for neo-adjuvant or adjuvant radiation or chemotherapy. An elderly patient presenting with a soft tissue tumor should therefore be thoroughly investigated to rule out the soft tissue sarcomatous conditions. It is very important to grade the tumor and patients should receive a full work up for staging.

CONSENT

Informed consent was obtained from patient for this case report.

ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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