

Metachronous Malignant Fibrous Histiocytoma- A Rare Case Report

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KEYWORDS	ABSTRACT
Metachronous, Malignant fibrous histiocytoma	Malignant fibrous histiocytoma (MFH) is one of the most common types of soft tissue sarcomas in adults. Distant metastases are developed in 30–40% of patients with MFH, with the most common site being the lung. However, metachronous MFH has not been reported previously in literature. This report describes a case of a 30-year-old man, who had two metachronous thigh tumors, both of which were confirmed to be MFH on histopathology and immunohistochemistry evaluations. A contemporary multidisciplinary approach to therapy including surgery, radiation and chemotherapy was advocated. Two primary sites of MFH raised the possibility of a genetic abnormality that could predispose such a patient to develop multiple primary sites of the same tumor.
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Introduction

Malignant fibrous histiocytoma (MFH) is one of the most common types of soft tissue sarcomas in adults, with the majority of tumors arising in the trunk or the extremities (1). About 30–40% of patients with MFH develop distant metastases, with the most common site being the lung (1). Metastatic disease in the absence of lung metastases is highly unusual (1). This report describes a case in which a patient had two metachronous MFH tumors without evidence of lung or other metastases. The patient had two primary sites of MFH, thus raising the possibility of a genetic abnormality that could predispose such a patient to develop multiple sites of the same tumor.

Case Report

We present the case of a 30-year-old man who originally noticed a progressively increasing swelling in his left thigh 6 years back. Magnetic resonance imaging (MRI) at that time revealed a soft tissue tumor in the left thigh, with no osseous destruction, and a core

needle biopsy confirmed high-grade MFH. (Figures 1(a) and (b)).

The patient was treated with neoadjuvant chemotherapy and underwent tumor resection followed by adjuvant radiation. He remained well until 6 years, when he noticed a 4x3x2 cm swelling in the upper right thigh associated with pain and progressive increase in size, with the present size of 10x6x4 cm. A digital skiagram revealed a pathological fracture in the proximal shaft of right femur. Multiple lytic lesions were noted within the proximal half of the shaft involving the medullary cavity and cortex with scalloping of the endosteal margin and focal destruction of the cortices. Surrounding soft tissue mass was seen. The MRI of the right femur revealed a lytic expansile mass within the femoral shaft involving the medullary cavity from subtrochanteric to middle-third of the shaft for a length of 22 cm with endosteal scalloping, cortical thinning and focal destruction of the cortex at many areas. A large lobulated heterogenous soft tissue mass postero-medially contiguous with the

medullary lesion via large cortical defect was seen in posterior cortex of the upper and mid-3rd junction of

femur. Radiological features were suggestive of a fibrosarcoma. (Figures 2(a), (b) and (c))

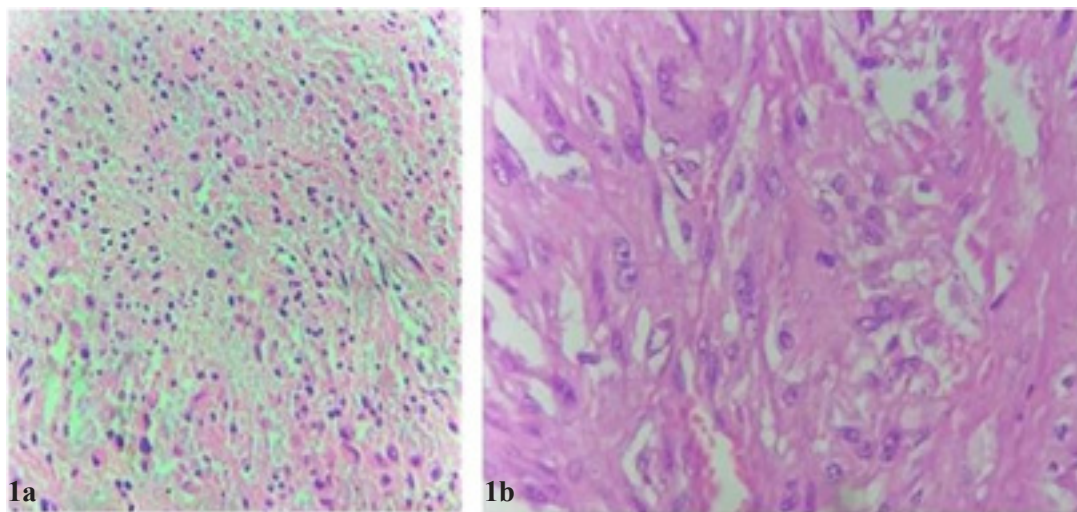


Figure 1. (a): H&E section (X10) and Figure 1(b): H&E section (X40) showing high grade MFH.

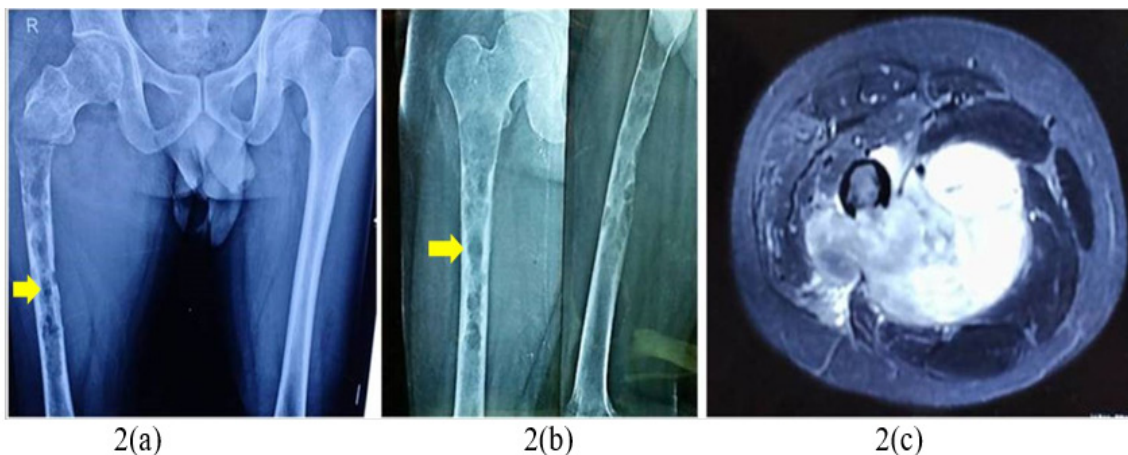


Figure 2. (a): X-Ray pelvis with B/L femur and Figure 2(b): X-Ray right femur showing lytic lesions. Figure 2(c): CT scan showing large lobulated heterogenous soft tissue mass.

Histopathology revealed a cellular tumor, with the cells arranged in a palisading and storiform pattern, consisting mainly of spindle to oval and round cells. The cells were showing moderate degree of pleomorphism, with formation of tumor giant cells. The cells showed very high mitotic rate, many of which were atypical. No bone formation could be identified in the tumor. However, the surrounding area showed fibroosseous callus formation. (Figures 3 (a) to (c)).

Differential diagnoses of MFH, osteosarcoma,

leiomyosarcoma, MPNST and poorly differentiated carcinoma were taken into consideration. On immunohistochemistry examination, tumor cells were positive for CD68, Vimentin [Figures 4(a) and (b)] and focally for SMA. However, SMA was negative in majority of the tumor cells as well as in the fascicles formed by the tumor cells (ruling out leiomyosarcoma), and tumor cells were negative for S-100 (ruling out MPNST), osteopontin (ruling out osteosarcoma), CK and EMA (ruling out poorly differentiated carcinoma).

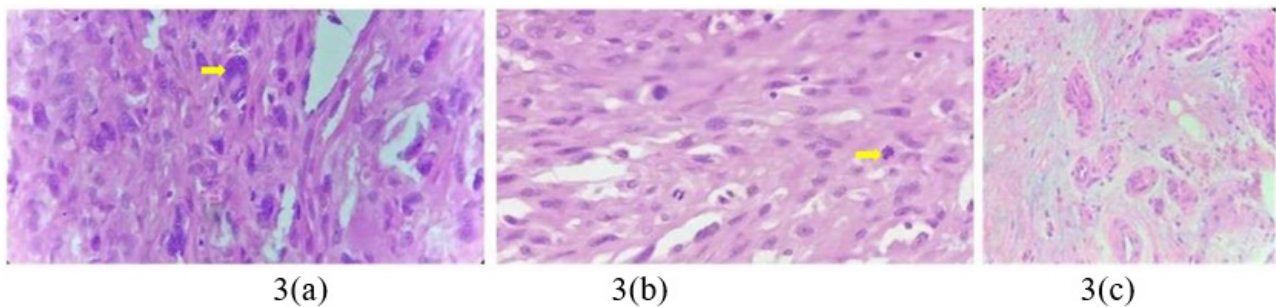


Figure 3. (a): H&E section (X40) showing bizzare atypical cells. Figure 3(b): H&E section (X40) showing atypical mitotic figures in a single field. Figure 3(c): H&E section (X10) showing formation of giant cells

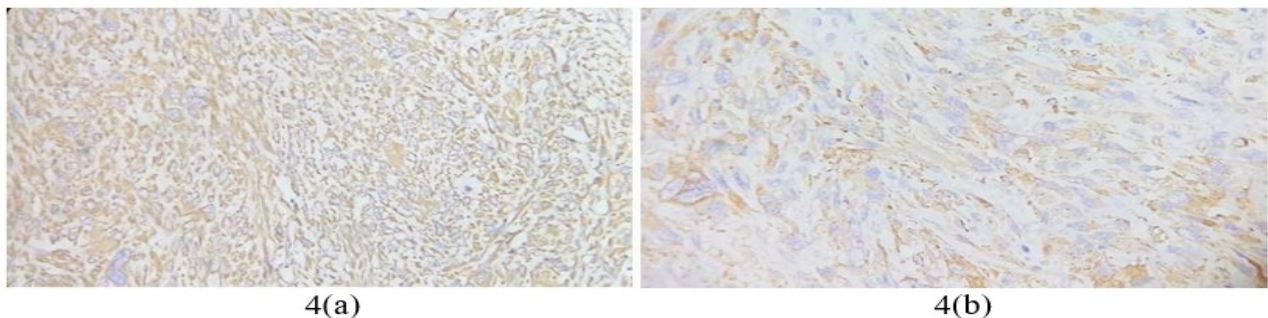


Figure 4. (a): Tumor cells showing positivity for Vimentin on IHC (X10). Figure 4(b): Tumor cells showing positivity for CD68 on IHC (X40)

Thus, a final diagnosis of high-grade MFH was made. Staging CT scans and PET scan preoperatively revealed no evidence of pulmonary, abdominal or other metastasis. The patient underwent neoadjuvant chemotherapy followed by wide excision of the right thigh lesion, which on biopsy was consistent with the diagnosis of high-grade MFH. The surgical margins of the resected thigh lesions were negative. Currently the patient is undergoing adjuvant chemotherapy and radiotherapy.

Discussion

Malignant fibrous histiocytoma (MFH) is considered to be one of the most common types of soft tissue sarcomas in adults, accounting for 36–40% of all soft tissue sarcomas (2, 3). The median age at diagnosis of MFH is 65 years (4) with peak incidence at 60–69 years (5). The most common primary sites were the extremities (77%), the trunk (15%) and the retroperitoneum (8%) (4). There are four major variants of MFH recognized today: storiform-pleomorphic (the most common), myxoid, giant cell and inflammatory (6). The local recurrence rate for MFH is 28–51%

depending on whether adjuvant radiation was used (3,7-10). The most common site of distant metastasis was by far the lung (63–91%), followed by lymph nodes (10%) and bone (3–8%) (7,8,11). Factors that are believed to favourably influence recurrence rates and metastasis in MFH include: small size, superficial location, increased proportion of myxoid component and low grade (5,12)

The case reported here showed an unusual feature of metachronous tumors, with two primary sites of MFH, located in soft tissues and bone of the extremities, without evidence of metastases to the lung parenchyma. There are two possible explanations for such an unusual clinical course: The reason why this patient did not have lung metastases was because of the two tumors represented separate MFH primary sites with a time interval of 6 years between them, i.e., metachronous tumors. However, to the best of our knowledge, there is only one case in the early original series on myxoid MFH which described a patient with multiple synchronous tumors on the arm, buttock and shoulder (5), and no case of metachro-

nous MFH has been reported previously. The second possibility is that the multiple lesions could have represented distant metastases. However, such a pattern without pulmonary involvement and with such a long time interval (6 years) between the two presentations is highly unusual. Moreover, the definition of metachronous tumors involves tumors at different sites, and at an interval of more than 6 months from each other. Hence, as these criteria are met, this is a case of metachronous MFH.

Advances in various techniques of chromosomal analysis have prompted many investigators to try and define MFH on a more basic molecular level. Earlier studies have revealed a clonal chromosomal abnormality in MFH, with further observation that the presence of an abnormal 19p+ marker chromosome was

associated with increased frequency of local recurrence (13,14,15).

Conclusion

In summary, we reported a case of metachronous MFH, with two primary sites and absence of pulmonary metastases. This, in turn, raised the possibility of a yet undetermined germ line mutation specific for MFH in such a patient, that could account for the development of multiple primary sites of the same tumor. Further studies aimed at determining the exact cellular aberrations associated with this neoplasm and their clinical significance are warranted.

Conflict of interest

All authors declare that there is no conflict of interest regarding the publication of this article.

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