

Case Report

Local recurrence of malignant fibrous histiocytoma 18 years after hemipelvic allograft replacement: a case report and review of literature

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Abstract: We report a rare case of very late local recurrence of malignant fibrous histiocytoma that occurred 18 years following initial treatment of the primary tumor wherein complete remission of the disease had been achieved. The patient had originally undergone a combined surgical mode of therapy immediately, and chemotherapy after the initial diagnosis, following which the patient was rendered disease-free. After a prolonged latent phase, the patient began to experience unexplained local symptoms. The patient was investigated at their local hospital where recurrence of the tumor was not initially considered as the cause of the presenting symptoms. After 18 years the patient was eventually referred back to the orthopedics department in Shanghai Tenth People's Hospital subsequent to the diagnosis of recurrent malignant fibrous histiocytoma being established. The patient has successfully undergone chemotherapy of the recurrent tumor and is receiving follow-up assessments at orthopedics department. We submit that this case highlights an under-appreciated need to remain vigilant for local tumor recurrence irrespective of the time of the initial diagnosis.

Keywords: Malignant fibrous histiocytoma, late recurrence

Introduction

Malignant fibrous histiocytoma (MFH), also known as pleomorphic-undifferentiated sarcoma (PUS), is a pleomorphic, aggressive highly complex, and high-grade sarcoma, composed of fibroblasts, myofibroblasts, and histiocytes. MFH is the most frequent soft tissue tumor of adults in later life and is most commonly found in the lower extremities including the retroperitoneal space [1]. In addition, presentation of MFH is secondary to other processes such as radiation, surgery, fracture, osteonecrosis, Paget's disease, non-ossifying fibroma or fibrous dysplasia in approximately 20% of cases [1]. MFH arising from a previous abnormality is usually more aggressive and has a poorer prognosis than primary MFH [2]. Primary osseous MFH is a central lesion found in the diaphysis or metaphysis of the bone that causes aggressive bone destruction and the appearance of a soft tissue mass. The most common sites are in the following order: the distal femur, proximal tibia,

proximal femur, and proximal humerus. Primary osseous malignant fibrous histiocytoma is less common. Presentation of MFH in the extremities occurs 70-75% of the time. In 50% of all cases, MFH appears in the lower extremities. Other less common sites include the retroperitoneum, the head, and neck.

The probability of inducing remission and curing MFH will depend on a variety of factors, including the presence of metastases, the size of the tumor, the anatomical location, the general health of the patient and other individual factors. Additional important factors to take into consideration include the manner by which the disease responds to treatment, the success of a reduced or ablated tumor debulking strategy by surgical and/or radiotherapeutic approaches, and the number of tumor cells that respond to chemotherapy.

Treatment of MFH depends on the grade, stage and the site of the tumor. Patients may also benefit from pre-operative chemotherapy be-

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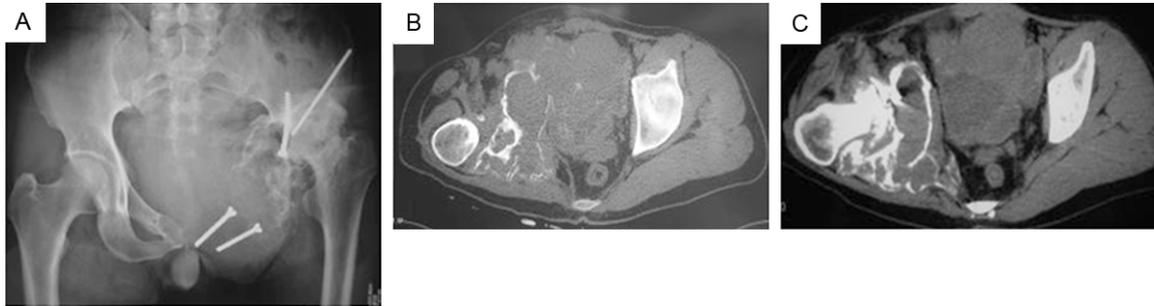


Figure 1. The image scans show the plain X-ray (A) and CT images (B, C) of the pelvis demonstrating a lytic lesion in the right acetabulum and pubis with a soft tissue component, while the original allograft is almost absorbed.

fore surgery and chemotherapy may also reduce the bulk of the tumor and increase the opportunity of a limb sparing procedure. In addition, to reduce systemic toxicity, selective trans-catheter intra-arterial chemotherapy has successfully been used in the management of this condition. However, local recurrence of the tumor is common [3], and treatment is similar to that of osteosarcoma [4]. The prognosis of MFH becomes more of a concern as the tumor lesion increases in size, invasiveness, and penetrance to the deeper areas of the soft tissues. Of greater concern, is the aggressive nature of MFH, which is known to metastasize to more distant anatomical sites including the lungs, liver, brain, heart, bone, and regional draining lymph nodes [5-10]. The reported five-year survival rate is described as varying widely from approximately 0-70% of cases [6-10]. This high variability in 5-year actuarial survival rate is in part due to the extremely malignant nature of MFH, particularly in older patients, and the somewhat preferable survival rates seen in patients younger than the fourth decade of life [6, 11, 12].

Case presentation

In 1994, a 44-year-old Han nationality male, farmer presented to his local hospital with a history of an enlarging and painful mass in his right hip and pelvis. At that time, plain radiographs suggested the diagnosis of a bone tumor affecting the right pelvis. Imaging was carried out at the local sarcoma unit where CT scans of the chest, abdomen, and pelvis were assessed. Examination of the scans revealed a suspicious lesion affecting the right pelvis with no evidence of distant metastases. A subsequent needle biopsy confirmed the diagnosis

of malignant fibrous histiocytoma (MFH). Concordant with these findings, AI chemotherapy (adriamycin and ifosfamide) was administered in late 1994. The chemotherapy regimen included adriamycin (75 mg/m^2) given as a continuous intravenous infusion for 3 days and ifosfamid given at 2 g/m^2 through d1-d4.

Although the patient was followed-up, this was not done regularly after the operation or following chemotherapy. The patient is a manual worker with an impressive endurance, and he did not demonstrate much discomfort. With the long term survival demonstrated by this patient, we had considered him cured. However, on this current clinical appointment, a plain radiograph of the pelvis was obtained after 18 years following the initial treatment. As the patient was disease-free for 18 years, he was discharged to the care of his general practitioner. In 2012, which was 18 years after the initial diagnosis, the patient suddenly developed pain and redness in his right hip with no history of trauma. The radiography illustrated a possible recurrence of the tumor. No improvement was observed from the first treatment, and consequently, he was not considered for further treatment.

The plain X-ray and CT scans of the pelvis demonstrated a lytic lesion in the right pubis with a soft tissue component (**Figure 1A-C**). Metastases of the lung were also detected. A needle biopsy confirmed the diagnosis of recurrent MFH. Six cycles of AI chemotherapy (ifosfamide, doxorubicin, DDP) were administered to the patient immediately following surgical operation. Histopathology examination confirmed the diagnosis of a recurrent MFH (**Figure 2**). The patient sustains active follow-up at the bone

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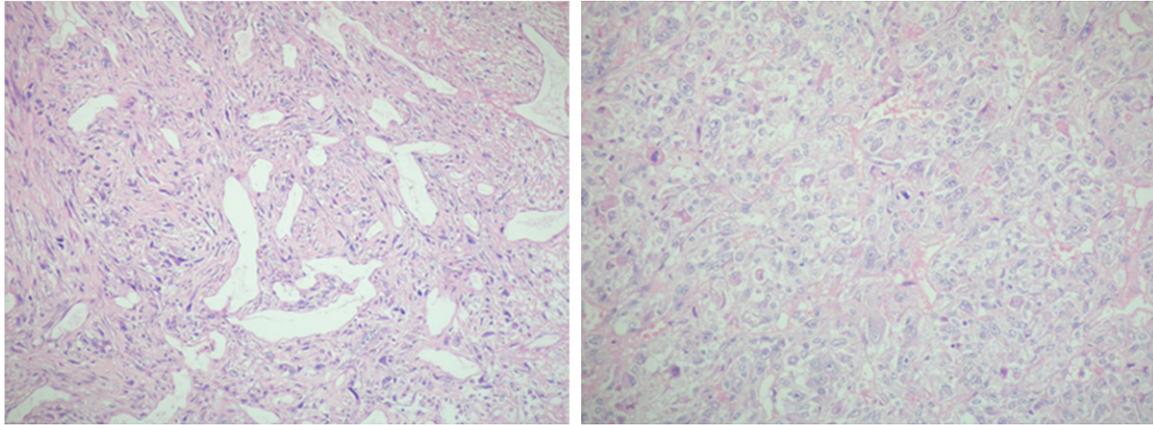


Figure 2. Pathological examination of the recurrent tumor.

and soft tissue sarcoma center in Shanghai Bone Tumor Institute.

Discussion

Clinic

Clinically, MFH presents with local pain and swelling. There is often a history of a rapidly enlarging mass. Pathologic fractures are present in approximately 20% of cases. By radiographic assessment, MFH presents as a highly aggressive, permeative lesion, which often lacks distinctive features found in other high-grade primary bone malignancies and is thus a highly undifferentiated soft-tissue malignancy. It usually presents with a soft tissue mass with or without cortical erosion [13]. In addition, there is usually no periosteal reaction [14]. By assessment of CT scans, the erosive, permeative destructive nature of the lesion is clearly observed together with evidence of soft tissue extension. Examination of CT scans is helpful in determining the extent of cortical erosion and intra-osseous extension. MRI findings in MFH are of intermediate signal intensity on T1 weighted images and of high signal intensity on T2 weighted images. Examination of MRI scans assists in defining the soft tissue mass, the bone marrow involvement, evidence of neurovascular structures and joint invasion. An inherent property of MFH is that it demonstrates increased uptake on bone scan which markedly assists demonstrate any evidence of tumor metastases [15]. From our experience, we believe that the reason why this patient could sustain such a long-term follow-up without recurrence was due in part to the initial wide

margin resection and high dose chemotherapy, which was started as early as possible.

Histopathology assessment

On gross examination, MFH is a lobulated, fleshy, gray white mass. There may also be yellow areas of lipid or darker areas indicative of hemorrhage. The mass may be all soft tissue or it may exhibit intra-osseous extension. The margins of the tumor are normally ill defined and destructive. By microscopic and histomorphology assessment MFH is usually characterized by intense poorly differentiated cellularity with pleomorphic nuclei, unusual mitotic events and the typical necrotic lesions common to these aggressive high-grade tumors [16]. In addition, there are five sub-types of MFH including storiform-pleomorphic, myxoid, giant cell, inflammatory and angiomatoid. In all forms of MFH, there are fibroblastic and histiocytic elements in the some ratio. The storiform-pleomorphic form of MFH accounts for 50-60% of all MFH and is normally found in large muscle groups of the extremity [16, 17]. Plump spindle cells are also found in a matted pattern in fascicles and a pinwheel pattern is found especially localized around the blood vessels. The myxoid form is hypocellular and has a large mucoid component. The giant cell form is characterized by necrosis and hemorrhage in addition to the presence of giant cells. The inflammatory form is typically characterized by the presence of many inflammatory cells including xanthomas, and is often found in the retroperitoneum. The angiomatoid form is often located in subcutaneous tissues. Additionally, MFH extends along fascial planes [15, 16]. Calci-

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fications are formed by reactive periosteal cells and are not produced by the tumor cells directly. This helps to differentiate the tumor from fibrosarcoma [3].

High-grade undifferentiated pleomorphic sarcoma is a relatively rare bone neoplasm that occurs in all age groups [18]. Several reports have described the effectiveness of neoadjuvant treatment for this condition, with a regime similar to that described for osteosarcoma [19]. Improvements in imaging techniques, chemotherapy, and surgical approaches have resulted in more limb-saving surgeries over the past three decades for patients presenting with osteosarcoma.

The recent literature has reported the response rate for chemotherapy and the 5-year survival rate as 56-62% and 66-76% respectively [20, 21]. Capanna et al. [22] reported that the 5-year survival rate for patients presenting with MFH improved from 28% to 57% upon administering chemotherapy with surgical treatment. Picci et al. [23] reported that a good pathological response was associated with much improved disease-free survival. In addition, the survival rates for patients presenting with osteosarcoma and MFH were quite similar although the response rate of patients presenting with MFH was significantly worse than that seen in patients with osteosarcoma [13]. We found only two reported cases of a malignant transformation of a neurofibromatous bone lesion to malignant fibrous histiocytoma [24, 25]. Moreover, only a small number of studies have specifically examined survival after recurrence in MFH [13, 14, 26]. From these studies, factors associated with superior survival included local recurrence only, lung metastases rather than extra-pulmonary disease, definitive surgery at the site of relapse, and relapse more than 2 years following the initial diagnosis.

Conclusions

The novel case described in this report, demonstrates the possibility of very late (18 years) local recurrence of malignant fibrous histiocytoma. In this patient, recurrent disease was not initially considered as an explanation of the new symptoms. In this case, the patient was treated with an extended duration of chemotherapy and irradiation therapy. However, the initial good response to treatment may have

resulted in some considerable delay in the clinical discovery of the recurrent disease found in this patient.

Disclosure of conflict of interest

None.

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