Oncological and Functional Outcome of Malignant Fibrous Histocytoma of Bone (MFH) of Upper and Lower Extremities Treated by Limb Salvage and Chemotherapy

AMR M.S. ABD EL-MEGUID, M.D.* and WALID A. EBEID, M.D.**
The Department of Orthopaedics, Faculty of Medicine, Bani Suef * and Cairo** Universities.

Abstract

Introduction: Malignant fibrous histiocytoma (MFH), a type of sarcoma, is a malignant neoplasm of uncertain origin that arises both in soft tissue and bone [1]. It was first described by O’Brien and Stout in 1964, as the most common tissue sarcoma in late adult life [1]. Malignant fibrous histiocytoma is a tumor rich in histocytes with storiform growth pattern.

Aim of Work: To asses the Oncological and Functional Outcome of Malignant Fibrous Histocytoma of Bone (MFH) Treated By Limb Salvage and Chemotherapy.

Material and Methods: This prospective random study was carried on 24 patients (16 males and 8 females), with age range from 8 to 62 years old, complaining from Malignant Fibrous Histocytoma of the upper and lower extremities. All cases were treated at Cairo University Hospitals from 1997 to 2007. All patients underwent wide surgical resection of the lesion and limb salvage using different modalities of fixations. Post-operative they also received different chemotherapy regimens depending on the time of entry to the study with a minimum follow-up period of 2 years. Patient functional outcome was evaluated according to the Musculoskeletal Tumor Society Functional Rating System (MSTS).

Results: After a minimum follow-up period of 2 years, functional outcome of the patients were satisfactory. Four patients suffered an isolated local recurrence, 3 had a local recurrence simultaneously with pulmonary chest metastases, and 7 patients had distant pulmonary metastases without local recurrence. Sciatic nerve lesion was observed in 1 case, 3 cases developed late postoperative infection. Among these 24 patients, 8 patient have die from chest metastases. Six patients were not available one year after surgery, and the remaining 18 patients, their functional score ranged from 20 to 30, (average score was 25).

Conclusion: We concluded that, proper surgical technique together with good chemotherapy regimens make limb salvage possible for patients with malignant fibrous histiocytoma of the upper and lower extremities. This procedure yields a good oncologic outcome.

Key Words: MFH – Limb – Salvage – Chemotherapy.

Introduction

MALIGNANT fibrous histocytoma MFH of bone, a pleomorphic spindle cell sarcoma which shares many features with certain subtypes of osteosarcoma, as a rare neoplasm [1]. MFH was described by O’Brien and Stout in 1964, is the most common soft tissue sarcoma of the late adult life [1]. In 2002 the World Health Organization (WHO) modified the nomenclature for soft tissue neoplasm, with the most significant changes being in the nomenclature for fibrous and lipomatous malignancies [2-4]. Originally, MFH was defined as a neoplasm showing both fibroblastic and histiocytic differentiation; however more recent evaluation has shown no evidence of true histiocytic differentiation. Further more the morphologic pattern seen with pleomorphic is shared by a variety of poorly differentiated malignant neoplasm [4]. For these reasons the WHO suggests new terminology for the various subtypes of MFH; several histological subtypes have been described [5]:

- Storiform, pleomorphic MFH (undifferentiated high grade pleomorphic sarcoma).
- Myxoid MFH, (myxofibrosarcoma).
- Giant cell MFH, (undifferentiated pleomorphic sarcoma with giant cells).
- Inflammatory MFH (undifferentiated pleomorphic sarcoma with prominent inflammation [6].

The clinical stage of the tumor, which is defined by tumor grade, size and presence of distant metastases, is the most prognostic factor. The anatomic site and depth of the primary tumor may also be of prognostic importance, but this is controversial [7]. Patients with low grade, intermediate grade, and high grade tumors have 10 years survival rates.
of 90%, 60%, 20% respectively. Patients with tumors less than 5cm at presentation have survival rates of 79-82% [7].

Patients with tumors of 5-10cm have survival rates of 62-68% and those with tumors larger than 10cm have survival rate of 41-45% [7].

Distant metastases most commonly occur to the lung (90%), bone (8%) and liver (2%) [7]. The overall survival rate of patients with MFH ranges from 36-58% at 5 years [7]. Malignant Fibrous Histocytoma (MFH) occurs more commonly in white patients than in patients of African or Asian descent. The male to female ratio is approximately 2:1. The tumor occurs with a peak incidence in the fifth and sixth decades but an age range of 10-90 years is reported [7].

Malignant fibrous Histocytoma (MFH) occurs most commonly in the extremities (70-75%), with lower extremities accounting for 59% of cases [8]. The most common clinical presentation is an enlarging painless mass in the thigh, typically 5-10cm in diameter [8,9]. Additionally, Malignant Fibrous Histocytoma (MFH) has been associated with haematopoietic diseases such as; Non Hodgkin Lymphoma, Multiple Myloma and Malignant Histocytoma. MRI is the imaging method of choice because of its ability to provide superior contrast between tumor and muscles, excellent definition of surrounding anatomy, and care of imaging in multiple planes [10,11]. Until 1970’s treatment for MFH and for other malignant bone tumors mainly relied on ablative surgery, with or without additional radiotherapy. Distant metastases developed in most patients treated in this way, resulting in poor long term survival approximately one third of the patients [12-14]. Such a combined local plus systemic treatment approach, usually based on existing protocol, has been associated with possible improved survival in non randomized settings [15-17].

The European Musculoskeletal Oncology Society (EMSOS) conducted a retrospective study to reach an experience of this unusual tumor. It was believed that such a combined European effort might lead to meaningful conclusion concerning prognostic variables and also to clarify the potential role of chemotherapy in the disease [17].

**Material and Methods**

This prospective study group included 24 cases with Malignant Fibrous Histocytoma (MFH) of bone, in the upper and lower extremities.

The lesion showed male predominance. 16 cases were males and 8 cases were females. Age ranged from 8 to 62 years old with a mean age of 36 years.

All cases were treated at Cairo University Hospitals from 1997 to 2007.

According to the site of affection, the commonly involved bone was the femur, 12 cases had the lesion in the femur, 8 patients were affected in the tibia, 2 patients had the lesion in the radius, while 2 patients presented with the lesion in the humerus.

Our diagnosis for the malignant Fibrous Histocytoma was based on.

Taking a full detailed medical history, radiological examinations and physical examinations, together with the following diagnostic tests:

Closed or open biopsy was done for all patients which confirm the diagnosis of malignant fibrous histocytoma, every case was staged according to its pathological findings. Biopsy is a surgical procedure that is usually performed in the operating room under sedation or anesthesia. High grade tumors are more aggressive, have a higher tendency to recur and spread. Low grade tumors are less aggressive and have a lower tendency to recur and spread. The grade is not a guarantee of a tumor’s behavior, but it is one of the factors that help us to make recommendations. The system used for staging system, is the surgical staging system developed by Enneking et al. (1986) and approved by the American Musculoskeletal Tumor Society [18].

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(Magnetic Resonance Imaging (MRI), to provide a superior contrast between the tumor, muscles, with excellent definition of the surrounding anatomy.

An angiogram, bone scan with technetium-99 was performed. These investigations showed that the tumor, in all cases, was intra-osseous without invasion of the soft tissues.)
All patients received post-operative chemotherapy treatment, according to a definitive chemotherapy protocols. Surgery, the lesions were approached, wide resection and fixation were performed using different modalities of fixations as follows:

Wide resection and fixation using modular prosthesis were performed in 10 patients, 6 with the lesion in the femur and 4 with the lesion in the tibia. Wide resection and pedicle fibular fixation method were done in 7 patients, 3 with the lesion in the femur and four with the lesion in the tibia.

Wide resection and rotationplasty were performed in one patient with femoral affection.

Two patients with the lesion in the femur were treated also with wide extensive resection, using the allo-prosthesis technique.

The two patients with the lesion in the radius were treated by wide resection and a non vascularized fibular fixation. Last 2 patient with humeral affection were treated also by wide resection and pedicled scapula. Wound was then closed on suction drainage.

**Case presentation:**
A 38 years old male patient with a malignant fibrous histiocytoma of the proximal tibia, treated by neoadjuvant chemotherapy and limb salvage using a modular endoprosthesis.

**Postoperative care:**
The patient was given antibiotics, sedation or analgesics for one week and restricted from all movements. Two days after surgery, the drains were removed, two weeks after surgery the stitches were removed.

Patients were discharged from the hospital after doing postoperative X-rays.

The mean follow-up period was four and a half years; it ranged from two years to 11 years. Patients were followed-up every 6 weeks, for six month, to assess the lesion and doing local X-rays, then every 3 months for 2 years.

Functional results and clinical assessment was done according to the Musculoskeletal tumor society scoring system (MSTS) [18]. This system
takes into account Pain, stability, motion, functional activity, strength and psychological status, which were all recorded.

Patients received one of the following chemotherapy protocols, these chemotherapy protocols were those used in the adjuvant treatment of osteosarcoma of bone [20]:

Protocol (1): In this protocol immediate surgery was performed followed by six courses of postoperative adjuvant doxorubicin (25mg/m²) and cisplatin (100mg/m²).

Protocol (2): In this protocol 2 cycles of neo-adjuvant doxorubicin (25mg/m²) and cisplatin (100mg/m²) were given then surgery was performed, followed by four cycles of doxorubicin/cisplatin in the same previous doses as postoperative adjuvant chemotherapy.

Protocol (3&4) s are shown in Figs. (1,2).

Response of treatment was evaluated by:

CT or MRI of the primary site of tumor, CT chest to detect any metastatic chest nodules and bone scans to detect distant bone metastases.

Patients were considered delayed in chemotherapy if they were delayed for more than one week and for more than one cycle of chemotherapy.

Results

The analyzed cases were 24 patients, 16 males and 8 females. Male to female ratio is 2:1.

The age range varied from 8 to 62 years. The mean age was 36 years. All were complaining from malignant fibrous histocytoma of long bones of the upper and lower extremities.

Average time of surgery was 3 hours, ranging from 4 to 5 hours.

All patients had wide resection margins, in one patient with malignant fibrous histocytoma of the distal femur, vessels was irresectable; graft to the artery was done using the saphenous vein as a graft.

Good Response: >=90% necrosis
Poor Response : <90% necrosis

Regarding the postoperative complications we had:

One patient had wound complication in the form of minor sloughing, which improved by repeated dressings and antibiotics.

One patient had sciatic nerve palsy, recovered in six months later.

Three patients had infection:

The first patient was a 12 years old female patient, had the lesion in the proximal tibia became early infected, 3 days post-operative.

The second patient was 57 years old male patient with lesion in the proximal femur developed infection one week post-operative, (the patient who developed sciatic nerve palsy).

The third one was a 45 years old male patient, had the lesion in the distal femur, had infection 10 days post-operative. All cases were managed by repeated dressings, antibiotics and regular follow-up, all these patients greatly improved.

we had 3 patients with pathological fractures, one patients had its fracture in the tibia, while the other 2 patients, pathological fractures were in the femur.
Local recurrence developed in 4 patients (about 17%), three of these four patients had simultaneous chest metastases and eventually died at 1, 2, 3 years intervals post recurrence.

Ten of the twenty four patients (about 40%) developed chest metastases. Five from these ten patients had chest metastectomy, but only two survive.

Out of twenty four patients, eight patients have die, from chest metastases.

Post-operative clinical assessment and functional results was analysed according to the musculoskeletal tumor society rating system (MSTS), this system (as discussed before) assess six parameters which are; pain, stability, motion, functional activity, strength and psychological status.

Six of our twenty four patients were not available for functional evaluation one year after limb salvage procedures due to oncologic complications, while the remaining eighteen patients were evaluated according to the MSTS system mentioned above.

The average follow-up period was four and a half years, ranging from two years to eleven years post-operative.

The functional score of the patients ranged from twenty two to thirty, with an average score of 25.

Discussion

In our study we represent a clinical experience of a series of patients with malignant fibrous histiocytoma of bone. The aim of this study was to gather information on the presentation, current treatment, and evaluate the outcome of this rare tumor after being treated with limb salvage surgery and chemotherapy.

Patients without adequate local control are highly unlikely to be long term survivors, regardless of other risk factors or treatment [21].

The rate of pathological fractures in our study is similar to that other reported series. We had 3 patients with pathological fractures, about 12.5%. This rate is similar to that reported by Stephen et al., 1999 who reported a rate of pathological fractures of 12% [21].

Limb salvage procedure has become the established mode of treatment of bone sarcoma in extremities. In our series we found that surgery done in this manner, combined with chemotherapy treatment achieved good functional outcome. Our average functional score, according to the Musculoskeletal Tumor Society Scoring System was 25, ranging from 20 to 30. This was similar to the functional outcome reported by Shishir Rastogi et al., 2004. They reported a series of 37 patients with high-grade sarcoma of upper and lower extremities, who underwent limb salvage procedures along with adjuvant chemotherapy and their average functional score was 23.2 [22].

Adjuvant chemotherapy for patients with malignant fibrous histiocytoma of bone is beneficial on prolonging survival and reducing the incidence of metastases. Results done by the Sarcoma Meta-analysis Collaboration in 1997 which included 1,600 soft tissue and bone sarcoma showed improvement not less than 10%. This percentage was found to be better in patients with extremity tumors than in patients with axial tumors [23]. The addition of supporting drugs such as hematopoietic growth factors has allowed for higher doses and trends in great improvement. The decision to incorporate chemotherapy in the treatment of malignant fibrous histiocytoma must be made with the guidance of medical oncologist [23].

On the other hand our oncological results corresponded well to other reported studies, which include smaller and larger groups of patients with malignant fibrous histiocytoma of bones of upper and lower extremities treated by limb salvage surgery and chemotherapy.

In our study, twenty four patients with malignant fibrous histiocytoma of bones of upper and lower extremities, treated with the same previous manner; four patients developed local recurrence (17%), ten patients developed chest metastases (40%), five from these ten patients had chest metastectomy but only 2 survived. Our average follow-up period was four and a half years ranging from two to eleven years.

Bacci et al., reported 12 patients with malignant fibrous histiocytoma of upper and lower extremities treated with limb salvage and adjuvant chemotherapy. After an average follow-up period of 10 months ranging from 6 months to 38 months, 3 patients had local recurrence (25%), 5 of the twelve patients had distant lung metastases (about 41%). All patients who had distant metastases died [24].

Another series was reported by Stefan Bielack et al., who reported 85 patients with malignant fibrous histiocytoma of upper and lower extremities treated with the same manner [22]. After a median
follow-up period of 3.9 months (ranged from 0.5 to 11.4 years), 33 patients had distant lung metastases (39%), while 8 patients only had local recurrence (about 10%) [21].

Conclusion:

We concluded that good oncologic and functional outcome could be achieved when treating malignant fibrous histiocytoma of bone by limb salvage surgery and chemotherapy.

References