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CASE REPORT

# Two Case-Reports of the Limb Salvage Treatment of Osteosarcoma Consolidated with Obvious Pathological Fractures

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**Abstract**
*Objective* The effect of the limb salvage of the treatment of Osteosarcoma Consolidated with Obvious Pathological Fractures is not very well, the purpose of this paper is to track the efficacy of limb salvage treatment when the patients accepted the artery intervention chemotherapy and enclosed 2 clinical case-reports.
*Methods* From January 2003 to September 2005, 2 clinical cases which one is a male, 29 years old, was confirmed osteosarcoma on the left distal femur, and the other is a female, 15 years old and has osteosarcoma on the right arm with obvious pathological fracture. After receiving arterial chemotherapy pump embedded, then started chemotherapy after the tumor biopsy, and the next process prosthesis replacement in limb salvage surgery after 5 times chemotherapy, follow on the next 5 times chemotherapy after the surgery.
*Results* With an average follow-up 70 months, there are no postoperative infection and prosthesis loosening found, also didn't detected tumor recurrence and metastasis, and the limb function recovered well.
*Conclusions* With the effective, neoadjuvant chemotherapy and comprehensive treatment, salvage treatment is not the contraindication of the patients with pathological fractures of combined primary osteosarcoma, and the treatment with long-term follow-up effectively.

**Keywords** Osteosarcoma · Pathological fracture · Limb salvage treatment · Chemotherapy

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## Patients, Methods and Results

Case one The first case was a male who, at age 29 years, was confirmed osteosarcoma on the left distal femur, and the cell type was osteogenic, at the stage of $II_B$ in January 2001, afrer some therapeutic regimen such as arterial chemotherapy continued irrigation, focused ultrasound ablation therapy, the pain and local tissue swelling has been significantly reduced. In October 2002, the patient appeared deformity and swelling in the lower left leg, also with increased pain and observed pseudoarthrosis. Other hospital diagnosed as "pathologic fracture of the left distal femoral", splinting for the treatment of more than 50 days but still in the doldrums, amputation was proposed to solve this situation but the patient refused. And then the patient transferred to our hospital in January 2003, the observation was the left thigh pain and with a great mass of local tissue, the local skin temperature increased and concomitant with shiny venous engorgement, the maximal tumor circumference was 47 cm and there are no systemic lymph node enlargement observed (Fig. 1). After one week, the patient underwent artery chemotherapy pump embedded in left

femoral, tumor biopsy, the pathology report as the osteosarcoma on the left distal femur, osteogenic, at the stage of $II_B$ (Fig. 2a) and bone traction of the left tibial tubercle, then started chemotherapy through arterial infusion after the operation (Fig. 3). The chemotherapy options is: cisplatin and doxorubicin chemotherapy by arterial infusion, while supporting with anti-repair therapy of caffeine, cisplatin (CDDP) 100~120 mg/m$^2$, epirubicin 60~100 mg mg/m$^2$, and supporting with caffeine (CF Anna Jia) 1~1.5 g/m$^2$ per 24 h after 2 h of cisplatin infusion, and maintain 72 h by chemotherapy pump, the chemotherapy will be executed 5 times before the limb salvage operation. After preoperative chemotherapy represented local pain vanish, the tumor significantly reduced, skin temperature decreased and the maximal tumor circumference reduced to 26 cm, X-ray examination showed soft tissue mass disappeared and the tumor/bone boundary clearly, fracture didn't healing (Fig. 4). In April 2003, the patient receiving left distal femur tumor section cut 25 cm and replaced with prosthesis (Fig. 5), Postoperative pathological diagnosis shows a great lot necrotic tissue red dyed but no structure and concomitance with hemorrhage, and also found necrotic trabecular bone among them, on the edge of necrotic tissue erupted some of the granulation tissue, no obviously activity tumor tissue traced (Fig. 2b). Postoperative recovered well and continue chemotherapy 5 times the same as before and periodic examination, after 77 months follow-up the X ray found no local tumor recurrence or distant metastasis (Fig. 6).

Case two This patient was a female, 15 years old. The patient's right arm swelling and pain after fall in June 2004, X-ray examination showed "fractured on the right humerus", for no restriction of activities the patient was not gave special treat, since then the arm existing persistent pain and particularly obviously at night, but can be tolerable. The pain became increasingly clear 2 months later and meanwhile the right upper arm soft tissue appeared obvious swelling, the local skin temperature higher than normal and the right shoulder joint activity was limited, given anti-inflammatory treatment but failed, the image diagnose shown as the malignant tumor on right upper humerus in September at the other hospital, the pain was significantly worse after then and the tumor growth rapidly. The patient was hospitalization to our hospital in October 2004, the observation was severe pain of right shoulder and with a great mass of local tissue, the local skin temperature higher and concomitant with shiny venous engorgement, the maximal tumor circumference was 45 cm, the right upper limb can't be activities (Fig. 7). Then the patient receiving chemotherapy of pump embedded in the right brachial artery and tumor biopsy, the pathology report as the osteosarcoma on right upper humerus, small cell type and at stage of $II_B$ (Fig. 10a). The chemotherapy option was as same as the first case before the limb salvage operation. This case represented local pain vanishes after 3 times

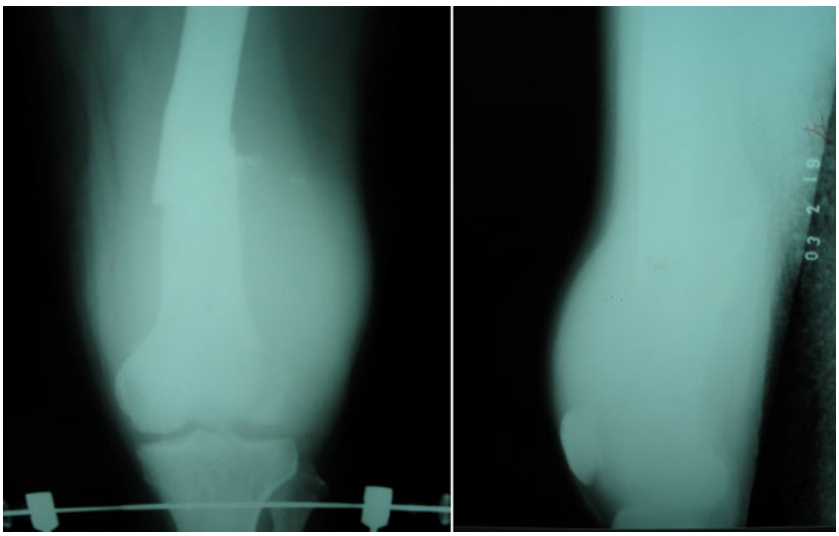

**Fig. 1** Left femur osteosarcoma with pathological fracture and large sofe tissue lump

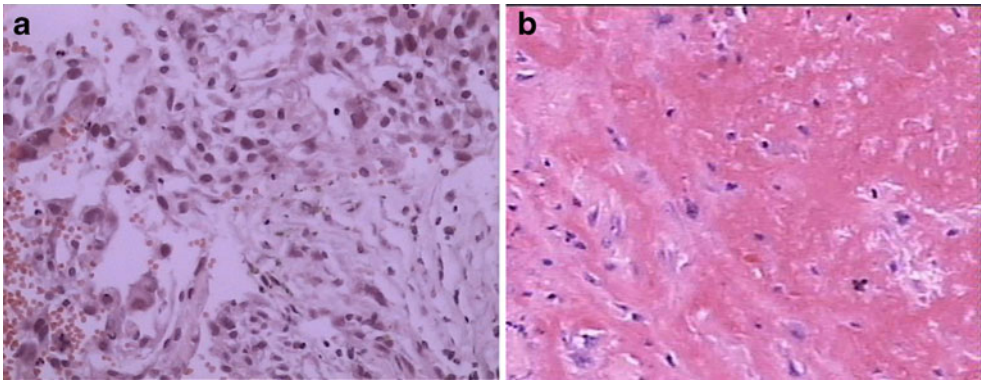


**Fig. 2** (**a**) Pathology of biopsy; (**b**) Anthology after chemotherapy and resection

preoperative chemotherapy, the local tumor significantly reduced 5 times latter, and the maximal tumor circumference reduced to 21 cm and the skin temperature recovered to normal, imaging showed disappearance of soft tissue mass, and the tumor/bone boundary definitionally (Fig. 8). The patient receiving left distal femur tumor section cut 17 cm and replaced with prosthesis after the chemotherapy (Fig. 9). The postoperative pathological diagnosis thinks the residual tumor cells synchronize with the response of II stage after chemotherapy (Fig. 10b) and then continues chemotherapy 5 times with the former scheme. Postoperative follow-up 63 months latter, the X ray found no tumor recurrence or metastasis detected (Fig. 11).

## Introduction

The advances in modern chemotherapy allow treatment strategy have a great breakthrough in patients with primary osteosarcoma. The 5-year survival rate of patients suffered from osteosarcoma with purely local treatment is merely 20 percent, along with the effective chemotherapy, the survival rate has been increased to 60 percent [1]. Although the limb-reserved operation has been gradually as the preferred treatment and the $II_B$ limb-reserved operation has been recognized, whether the osteosarcoma consolidation of pathological fracture could carry out limb salvage surgery is still the focus of the debates [2].The incidence of pathological fracture at diagnosis or during neoadjuvant chemotherapy in patients with osteosarcoma ranges from 5% to 12% Previously identified risk factors for pathologic fracture

**Fig. 3** Chemotherapy by affiliated Intra-artery

**Fig. 4** Soft tissue lump disappeared through 5 times chemotherapy

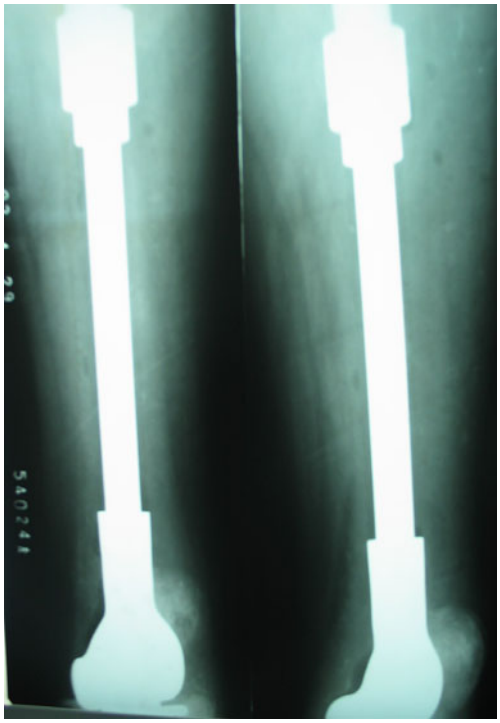

**Fig. 5** Left femur constructed by prothesis replacement

are site (proximal location), location in affected bone (diaphysis), radiographic pattern (osteolytic), an unusual histologic subtype (telangiectaticor fibroblastic), and a large tumor size. Clinicopathologic variables of major concern regarding the prognosis of pathological fractures caused by osteosarcoma are histologic subtype, tumor size, location, histologic response, and local recurrence [3–5]. Preoperative chemotherapy has been effectively reduced tumor border, probably also lead to the healing of fractures, but the effect of fracture healing in patients with osteosarcoma and the prognosis is still uncertain [6]. We have been successfully treated 2 pathological fractures in patients with osteosarcoma through effective limb salvage treatment and chemotherapy.

## Conclusion

About 5% -20% of patients suffered from osteosarcoma occured pathological fracture in the preoperative treatment [7, 8]. For the high active, poorly differentiated osteosarcoma cells and damaged trabecular system, pathologic fracture of primary malignant bone tumor often caused by spontaneous or trauma scores. If the local tumor blood supply affluently, the capillary will be proliferated and along with osteolytic changes in the limb bones, the patients prone to pathologic fracture. Therefore, the coalition of pathological fractures is one of the performances of the extremely malignant osteosarcoma. Malignant bone tumor with pathologic fracture often leads to hematoma formation, can be spread or pollution to nearby soft tissue, neurovascular bundles or joints, the used treatment was amputation to avoid the proliferation of tumor cells. With the gradual development of neoadjuvant chemotherapy, many researchers have been reported it is feasible to salvage the limb in the pathological fractures of osteosarcoma therapy.

Compared with limb salvage treatment, Abudu et al (1996) [8] think that amputation is a radical resection method to local tumor, but cann't prolong survival time. The 5-year survival rate of patients suffered from osteosarcoma was approximately 60 percent. Many osteosarcomas with merged pathological fracture can be resection margin adequately and won't endanger the patient's survival through some limb salvage surgery treatment, but there is the possibility of high-risk relapse. When the patients receiving effective chemotherapy, the local recurrence rate of the limb salvage treatment about the osteosarcoma consolidation of pathological fracture was 19 percent, the patients who had the amputation had no recurrence of the word. 2000, Zeifang et al [9] made a retrospective analysis about the 30 cases of merged pathological fracture of the treated 336 cases patients suffered from osteosarcoma, point out that patients with merged pathological fracture were more than 2 times risk of death than patients who without, and think that limb salvage treatment does not affect the survival rate.

2003, Mayil et al [10] reported that the surgery treatment of the osteosarcoma with pathologic fracture was similar to

**Fig. 6** Followed-up by 77 months with no loosening and lacal recurrence

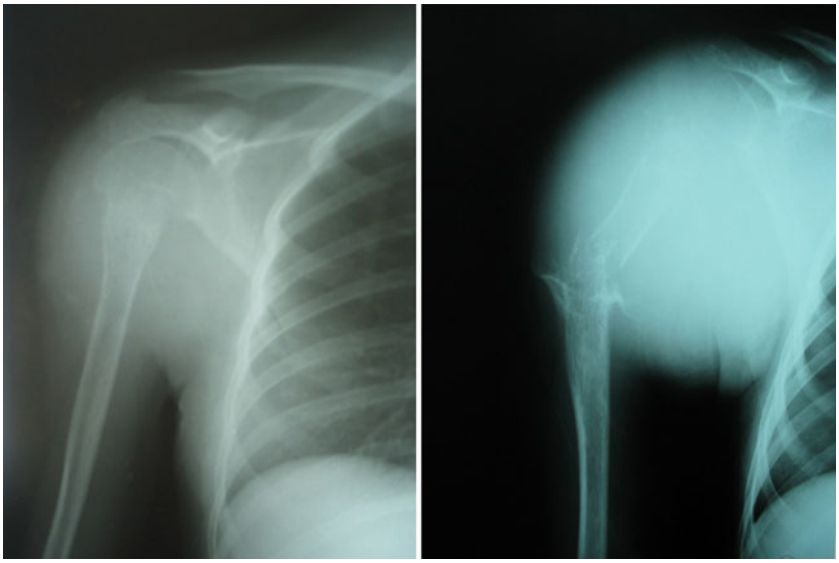

**Fig. 7** Right humerus osteosarcoma with pathological fracture and large sofe tissue lump

the treatment about the osteosarcoma without pathologic fracture by the supporting of new adjuvant chemotherapy, and the local salvage treatment won't increase the risk of recurrence or death. Among the treated patients who had osteosarcoma associated with pathological fracture, the local recurrence rate was only 11 percent, same as the treated patients suffered from osteosarcoma without pathologic fracture, the local recurrence rate of osteosarcoma consolidation of pathological fracture which underwent the limb salvage operation did't increase, the chemotherapy can get a satisfactory and clarity surgical borders, while ensuring the survival time. The same year, Bacci et al [11] through follow-up the treated 735 cases of osteosarcoma, point out that in the case of effective chemotherapy, there were no significantly different between the 5-year disease-free survival time and the total survival time with or without pathological fracture.

Walid et al [12] point that, merging pathologic fracture of primary osteosarcoma was considered as a contraindication of limb salvage treatment lies in two aspects, one was the fracture will cause the local hematoma formation, which is conducive to tumor cell spread to adjacent tissues and subsidiary joints, the other was that the microcirculation damage is more conducive to the transfer of the tumor. But the limb salvage surgery is still feasible through effective neoadjuvant chemotherapy, preoperative chemotherapy and appropriate application of the reconstruction mode. In recent years, many domestic scholars affirmed the effect of the limb salvage operation about the patients suffered from osteosarcoma with pathological fracture [13, 14],

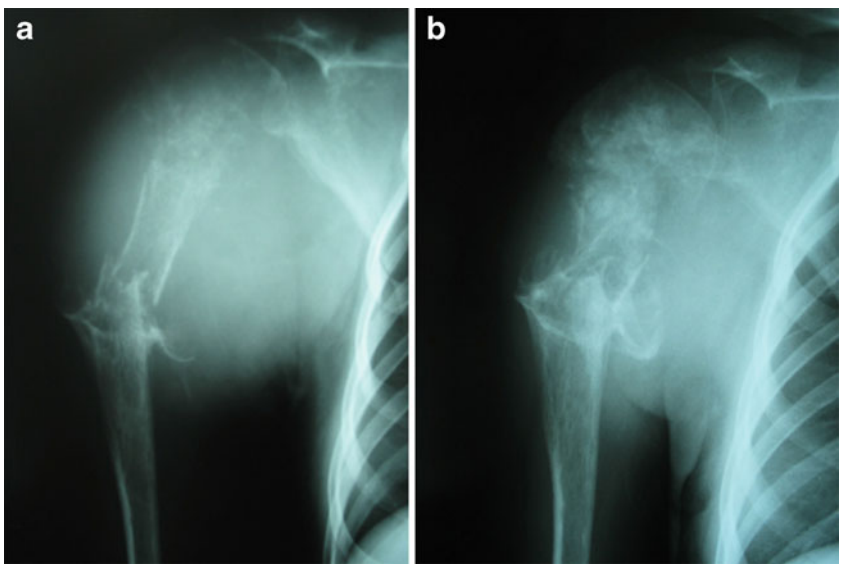


**Fig. 8** (**a**) Soft tissue lump grew downwards through 3 times chemotherapy; (**b**) Soft tissue lump grew downwards obviously through 5 times chemotherapy

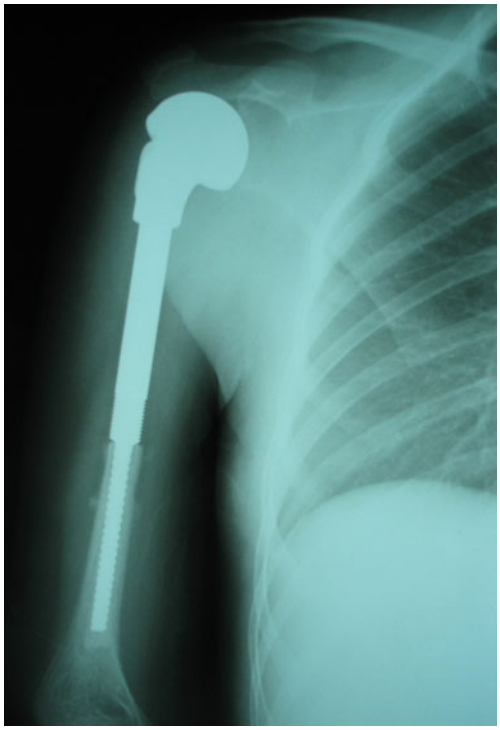

**Fig. 9** Right humerus constructed by prothesis replacement

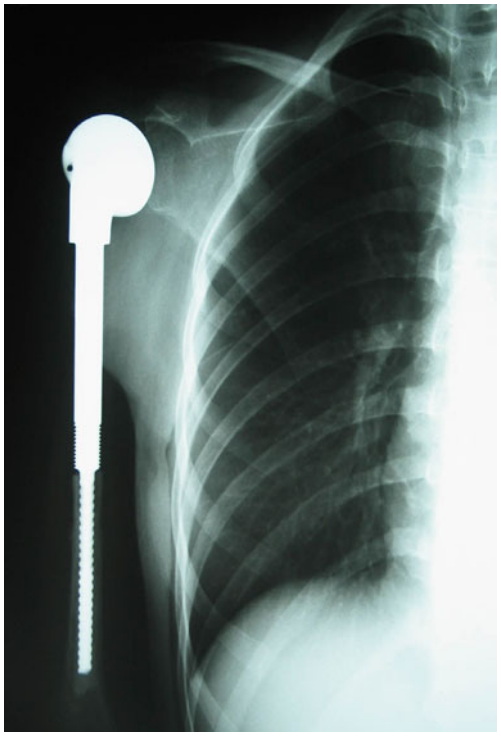

**Fig. 11** Followed-up by 63 months with no loosening and lacal recurrence

patients who sensitive to chemotherapy and even if occurred the fracture, it is also feasible to execute completly tumor resection and prosthetic replacement after the chemotherapy and appropriate treatment, and also could be obtain good local control and reduce the incidence of lung metastasis.

These scholars emphasized that after the effective chemotherapy, the osteosarcoma with combined pathological fracture was no longer be a single amputation of surgical treatment, to achieve the limb salvage purpose by a reasonable local excision, it was also did'n affect the survival time of patients. The two cases of the patients suffered from osteosarcoma which we reported that with obvious pathological fracture, with mean follow-up 20 months after the limb salvage treatment, all were no local recurrence or metastasis of the tumor. No local recurrence of tumor mainly depends on the application of the new adjuvant chemotherapy, which on one side used the artery chemotherapy Pump infusion, to increasing the local concentration of chemotherapy drugs, concentration of chemotherapy drugs and their effect concentration has an obvious dose-response relationship within a certain range, when the chemotherapy drugs concentration of each increased by 1 times, its effect is increased by about 10 times; on the other hand,

We supporting with the caffeine to enhancing the ability of cisplatin, adriamycin and other genotoxic anticancer, antineoplastic agents to kill tumor cells. Caffeine can increase the

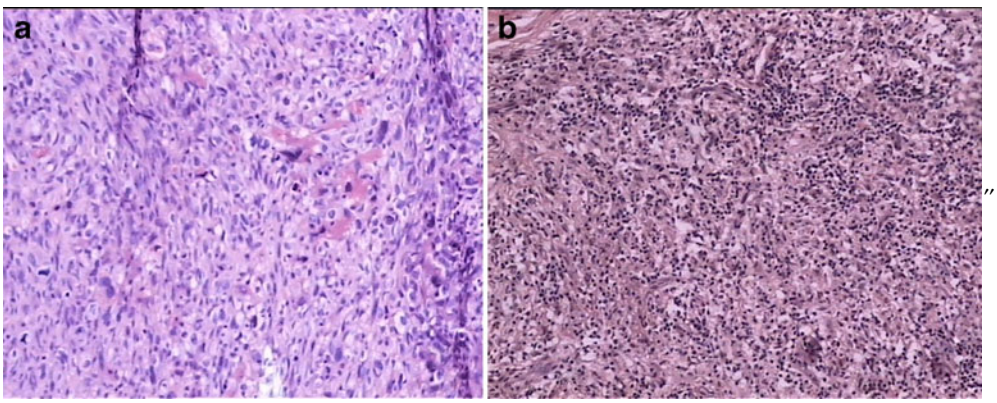


**Fig. 10** (**a**) Pathology of biopsy; (**b**) Pathology after chemotherapy and resection

effect of cisplatin and the other antitumors 10 to 300 times, through the intervention of tumor cell's cycle control and lead to apoptosis of tumor cells [15]. As we all know, osteosarcoma on physically remote is currently take the neoadjuvant chemotherapy combined with derivation to induced apoptosis of tumor cells, both of which were the important prognostic factors affected the local tumor recurrence. 2001, Eliber et al [16] reported that treatment of induced tumor cell apoptosis was the important factor to predict the survival time of those patients who received neoadjuvant chemotherapy and the possibility of tumor's local recurrence. If the sarcoma cell necrosis rate of the well-differentiated soft tissue on distal limb was much than 95 percent, the 10-year local recurrence rate of the tumor was 11percent, if the sarcoma cell necrosis rate was less than 95 percent, the 10-year local recurrence rate of the tumor will be 23 percent.

Based on the clinical results, the occurrence of pathological fracture did not increase the risk of local recurrence of the osteosarcoma on distal limb. Patients suffered from osteosarcoma with pathological fracture, with the application of effective chemotherapy, the local tumor could be controled and to execute the limb salvage treatment, and the long-term follow-up effectively.

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