CASE REPORT

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The interdisciplinary approach of an aggressive giant cell tumor of bone complicated with a fracture of the distal femur

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Abstract

Giant cell tumor of bone (GCTB) represents one of the commonest bone tumors encountered by an orthopedic surgeon. The giant-cell tumor is generally classified as benign but the fast growing rhythm and the aggressive soft-tissue invasion may in some cases demonstrate a malign potential of the tumor. We present the case of an aggressive giant cell tumor in a young patient that was first diagnosed in our emergency department with a fracture of the distal femur after a low energy trauma. With further examinations, we discovered that the tumor was invading the both femoral condyles and was vascularized by three major arterial pedicles. The onset of his problems was the femoral fracture and the changes on the major vessels, muscles and nerves. After an interdisciplinary approach of the patient and a meticulous preoperative planning, we decided to make an extensive total resection of the tumor followed by a complex reconstruction surgery for the bone. A very stable fixation of a vascularized graft allowed the bone to heal even if the surrounded soft-tissue was almost completely invaded by the tumor and removed during the excision. The follow-up of this case demonstrated that using an interdisciplinary approach of the patient with the Plastic Surgery team, we manage to remove the tumor within oncological limits and achieved bone healing with good stability of the distal femur.

Keywords: giant cell tumor, pathologic bone fracture, vascularized fibular graft, reconstructive microsurgery.

Introduction

Extensive local excisions of skeletal tumors in the knee region create reconstruction problems with several alternative solutions. Difficulties in local control of giant cell tumor (GCT) of bones as well as high rate of local recurrence following initial surgery have led the investigators to use different surgical modalities for the treatment of GCT according to stage of the disease aiming at decreasing the rate of local recurrence with good functional and cosmetic results [1]. Giant cell tumors are typically located in the meta-epiphyseal region, often extending to the articular subchondral bone or even abutting the cartilage. These lesions are thought to arise in the metaphysis and extend into the epiphyseal region after physeal closure. In the rare instances when GCT occurs in skeletally immature patients, it will be located in the metaphysis. The surgeon needs to strike a balance during treatment between reducing the incidence of local recurrence while preserving maximal function of the limb [1–3]. Custom-made endoprostheses now compete with joint homografts and fusion with autogenous bone grafts. Extensive osteo-articular allografts have been used for knee reconstruction, but because of their composite nature and the technical difficulty of the procedure, complication and failure rates reported in literature have been high [4]. Under such circumstances, it is necessary to maintain length of the involved extremity, and provide a skeletal stability in the area of resection.

Most of the cases with CGT needs an interdisciplinary approach for a successfully treatment, especially when the tumor starts to invade both soft tissue and bone. Surgical management of the tumor is represented by oncological resection of the tumor and musculoskeletal reconstruction of the area involved. The most frequent localizations of the GCT are the distal femur but they may also invade the proximal humerus, proximal tibia or distal radius.

Being involved in the knee joint, the distal femur has an important role in lower limb biomechanics and for this particularly cases a well prepared planning is necessary [5].

We are presenting the case of a giant cell tumor of bone (GCTB) located in the distal femur and complicated with a fracture after a low energy trauma. The particularity of the case is the aggressive type of the tumor and the association of a pathological fracture.

Case presentation

A 34-year-old male patient accused pain and functional impotence and he also complained of progressive swelling of the left knee joint for last few years without preceding history of trauma to the knee joint. He did not have a history of fever, chest pain, other joint swelling. He had not taken any kind of treatment and never went for a medical consult. The patient was hospitalized immediately in the Department of Orthopedics and Traumatology for the fracture treatment. After the written informed consent was obtained from the patient, we started the investigations and the preoperative planning in an interdisciplinary approach.

On clinical examination, there was diffuse swelling of the knee joint more on the distal femur and pain in

context with the current trauma. The range of motion in the knee was totally limited but the distal neurovascular status was intact. On standard radiographs of the knee, which is seen in Figure 1 [anteroposterior (AP) and lateral view], there was diffuse expansible radiolucent lytic lesion with cortical breach and a supracondylar fracture of the femur. Usually, this kind of fracture is associated with secondary injuries due to the high-energy mechanism but not in cases with bone weakness.

The patient was hospitalized immediately in the Department of Orthopedics and Traumatology for surgical treatment. After temporarily stabilized the fracture with a long leg splint, we started the investigations of the patient and the preoperative planning in order to make possible the first surgical intervention.

The blood tests showed no signs of significant blood loss after the femoral fracture as shown typically. The patient's general condition was good and we performed other laboratory tests in order to find any other secondary dissemination. The knee magnetic resonance imaging (MRI) showed that the tumor had the starting point in the bone and was invading the local soft tissue in an aggressive manner. We performed computed tomography (CT) of the thorax, abdomen and pelvis that shown no signs of metastasis knowing that benign giant cell tumor of bone can produce pulmonary metastases (Figure 2). We also did a full-body scintigraphy test that showed increased concentration of the tracer just above the knee joint and no other secondary localization (Figure 3).

The patient was prepared for biopsy examination under loco-regional anesthesia. The harvested fragment from the tumor measured 1.5 cm/1 cm was friable with a brown-hemorrhagic aspect. The piece was fixed in 10% buffered formalin for 24 hours and processed in paraffin. The microscopic examination showed that the tissue fragments collected from the tumor formation revealed a multinucleated giant cell tumor proliferation, relatively uniformly distributed and mononuclear cells relatively monomorphic, with typical present mitosis (five mitoses/10 HPF – high power field); also, areas of hemorrhage and tumor necrosis were present (Figure 4). There were no signs of sarcomatous aspect or tumoral necrosis and this has excluded malignancy of the tumor directing us to an aggressive GCTB (Figure 5).

Even if the patient's general condition was good and there was no other signs of secondary metastases, the local evolution of the tumor is similar to malignant tumors of the distal femur: osteosarcoma, fibrosarcoma, chondrosarcoma. Bone resection is not usually recommended because of its significant morbidity. It is only indicated in proximal radius and fibula and distal ulna, tubular bones of hand and foot, coccyx, sacrum and pelvic bones, also in situations in which their reconstruction is not possible as in some patterns of pathological fractures and massive involvement with an incomplete shell of cortex that is insufficient to contain cement.

The options for the surgical type of treatment were: the middle thigh amputation with prosthesis or the oncological resection with soft tissue and bone reconstruction or the segmental defect after totally tumor resection in oncological limits and orthoplastic reconstruction.

Then, lower limb arteriography was performed which revealed three major vascular sources of the tumor can thus be embolized (Figure 6). In this way, the main surgery consisted in tumor resection in oncological limits could be done safely. Intraoperative appearance of the tumor after a cautious dissection of the adjacent tissues can be seen in Figure 7a.

Due to its classification (3rd grade), the tumor has been removed in two steps (Figure 7b) and the bone defect was filled with poly(methyl methacrylate) (PMMA) (Figure 7c). The fracture was stabilized with a locking condylar plate 4.5 mm and the articular surface was completely preserved. Following the intervention, the knee was immobilized in a splint and no weight bearing was allowed for the leg.

We sent the tissue fragments harvested from the bone and from the tumor with sizes between 2 and 3.5 cm. They had brown-hemorrhagic aspect and irregular shape. The total volume of material was about 200 cm^3. The fragments were fixed in 10% neutral formalin for 48 hours. The bony fragments were decalcified in a 15% nitric acid solution for 48 hours. After this process, the fragments were processed to paraffin with 5-µm sections using Hematoxylin and Eosin (HE) staining.

The histopathology examination after the full resection of the GCT tumor revealed a tumor proliferation of similar appearance, consisting of multinucleated osteoclast-like giant cells uniformly distributed and oval and elongated stromal cells arranged in storiform pattern. Also, vacuolar aspect macrophages and lymphocytes were present. Stromal cells do not show atypical changes and the mitosis was relatively low (about five mitoses/10 HPF) without atypical mitosis.

After a period of 10 weeks, we prepared the patient for the second surgery represented by the microsurgical transfer of a vascularized fibular graft and addition of non-vascularized bone graft from bilateral posterior iliac crest. Thus, fibular graft was fixed with a full threaded 4.5 mm screw keeping the biomechanical axis of the femur (Figure 7d). The iliac crest bone graft was integrated in the biomembrane created by the cement (Masquelet technique).

The tumor was diagnosed accidentally after a low-energy fracture and even if the patient felt the swelling above the knee for several years, he never went to a medical consult. Histopathological examination confirmed the GCTB suspicion raised on the imagistic tests.

The treatment consisted in total resection within oncological limits and the musculoskeletal reconstruction was based on the microsurgical transfer of the fibular graft and the 4.5 mm locking condylar plate osteosynthesis.

We managed to diagnose and treat a pathological bone fracture of the distal femur with a GCT in a short period of time using an orthoplastic approach. The major complications that we avoided were resorbing of the graft, infection, articular surface collapse and tumor recurrence.

The patient started partial weight-bearing motion three months after the last surgery when the radiological aspect showed the first signs of bone union. After another six months, the fibular graft grew in thickness and no other clinical and paraclinical signs of tumor spread were present (Figure 8). After 12 months of follow-up, the patient walks with full-weight bearing and we did not see any signs of tumor recurrence. We analyzed the range of

motion in the knee and our last examination showed that the patient can do full-extension, 90^0 flexion and no signs of knee instability (Figure 9).

A very stable fixation of the vascularized graft allowed the bone to heal even if the surrounded soft-tissue was almost completely invaded by the tumor and removed during the excision within oncological limits.

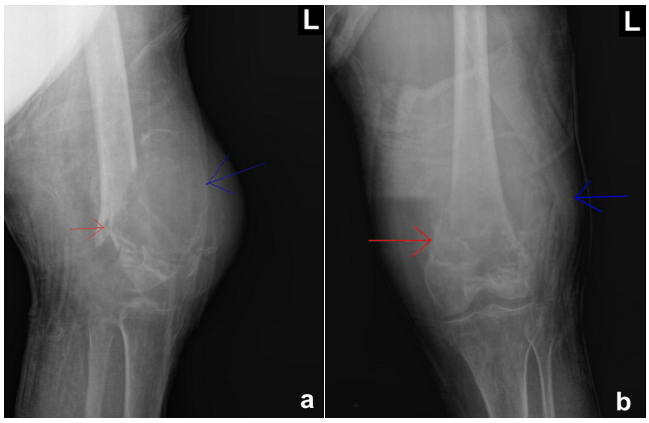

Figure 1 – *Initial X-ray examination of the knee showing a supracondylar fracture of the femur, probably on a pathological bone and a lytic eccentric lesion: (a) Antero-posterior (AP) projection; (b) Lateral projection.*

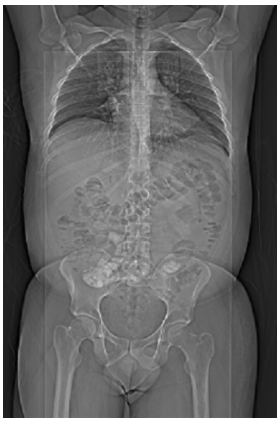

Figure 2 – *CT scan of the thorax, abdomen and pelvis showing no signs of secondary metastasis.*

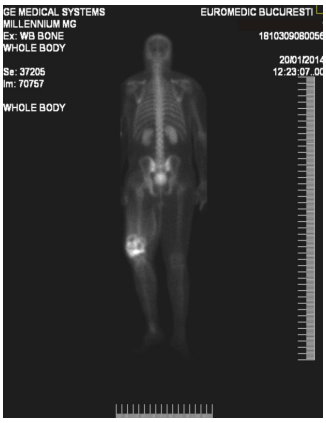

Figure 3 – *Scintigraphy test: we can observe that the concentration of the tracer is significantly increased in the lower thigh.*

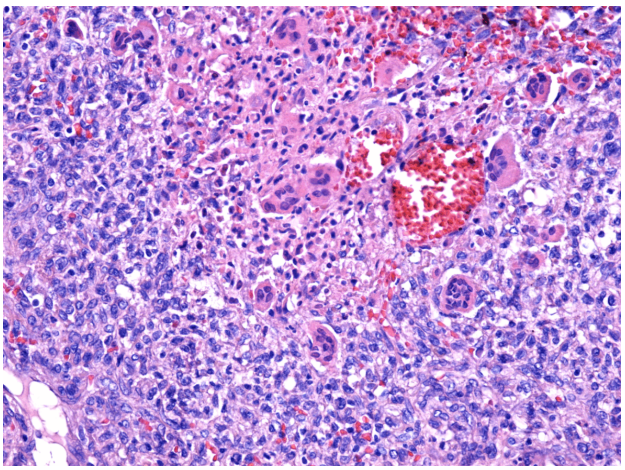

Figure 4 – *Initial biopsy examination infirming the clinical suspicion for malignancy. The result of the exam: multinucleated giant cell tumor proliferation with typical present mitosis (five mitoses/10 HPF). HE staining, ×200.*

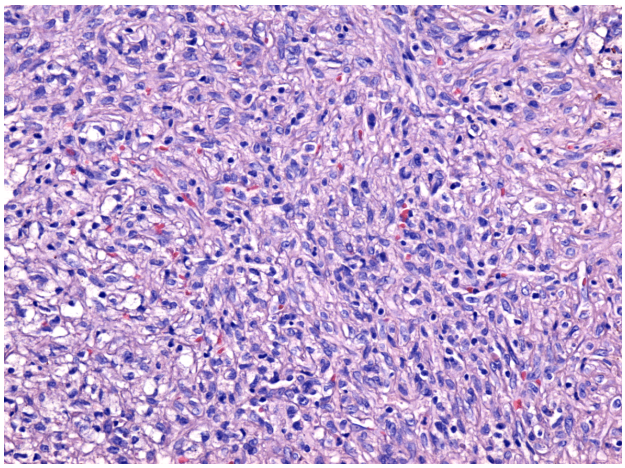

Figure 5 – *Secondary histopathology examination of the tumor after the first surgery. The result of the exam is: stromal cells do not show atypical changes and the mitosis were relatively low. HE staining, ×200.*

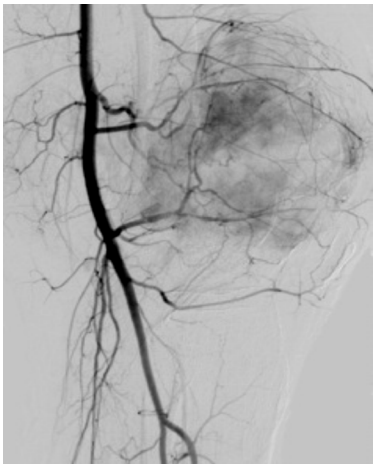

Figure 6 – *Angiogram of the left popliteal artery shows the increased vascular supply of the tumor.*

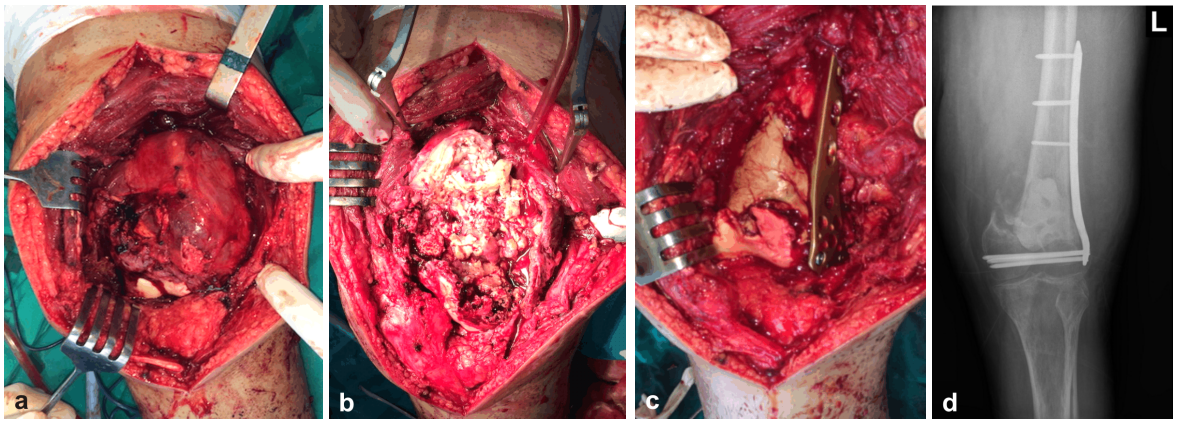

Figure 7 – ***The first surgical intervention – intraoperative aspect: (a) Clinical aspect of the tumor; (b) Pathological bone aspect; (c) Bone defect filled with cement and stabilized with a 4.5 mm interlocking plate; (d) Postoperative X-ray examination: LCP (locking compression plate), the cement that filled the defect and the good alignment axis.***

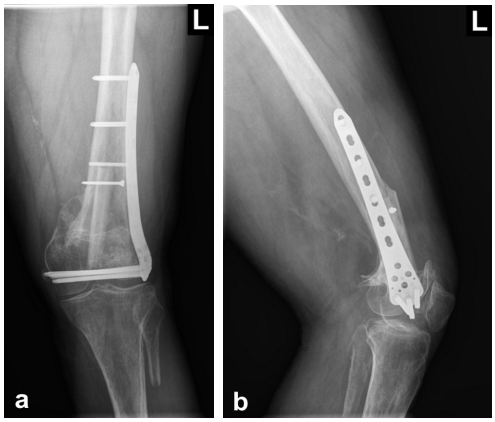

Figure 8 – ***Radiological aspect of the knee 12 months of follow-up showing a thicker fibular bone graft and the fracture union: (a) AP projection; (b) Lateral projection.***

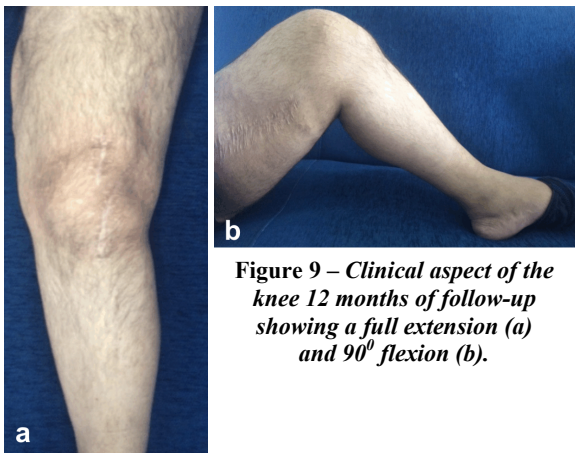

Figure 9 – ***Clinical aspect of the knee 12 months of follow-up showing a full extension (a) and 90^0 flexion (b).***

Discussion

Many injuries were diagnosed in the past as GCT: non-ossifying fibroma, chondromyxoid fibroma, chondroblastoma, Langerhans cell histiocytosis, solitary bone cyst, aneurysmal bone cyst, osteoblastoma. The factors that oriented us toward the diagnosis of GCT were: the clinical context, the tumor location, imaging examinations, the spatial relationship between giant cells and stromal cells and the absence of osteoid tissue [5]. The tumor location in the distal femur is very frequent, some studies demonstrates that 30% GCT of bone occur in distal femur, 20% occur in proximal tibia, 20% in the distal radius, 10% distal ulna, 10% proximal femur, 7% proximal humerus and 3% in the calcaneum [6]. The treatment is very challenging at this level and can lead to knee arthrodesis or even thigh amputation [7].

First described by Sir Astley Cooper, in 1818, as a benign bone tumor, giant cell tumor of bone tumor proliferation is now considered a low grade malignancy due to its tendency to relapse and metastasis capacity; described as somewhat separate entity, giant cell tumor is considered malignant when frankly sarcomatous stromal cells along with other histopathology characteristic aspects are involved [8–10].

Imaging studies are essential for the diagnosis of GCT and can also identify possible tumor recurrence after total resection. On conventional radiographs, this tumor typically presents as a purely lytic eccentric lesion, with expansion and thinning of the cortex. Periosteal reaction is usually absent [11, 12].

GCT of bone is a locally aggressive tumor with a high tendency to recur after removal. The rates of recurrence after simple curettage ranged from 12–65% as compared with 12–27% after curettage and adjuvant treatment and 0–12% after resection. In cases of GCT affecting the hand and foot, the recurrence rate is higher in comparison with GCT in more conventional sites. Most commonly, the metastatic spread occurs after repetitive local recurrences [13–15].

Campanacci *et al.* classified GCT in three grades: grade 1 is static form with minimal involvement of the cortex, grade 2 presents with thinned and expanded cortex, and in grade 3 the lesion penetrates the cortex and has a soft tissue component as in our case report. For this reason, the tumor was resected in two large fragments during the first surgical intervention.

Difficulties in local control of GCT of bones as well as high rate of local recurrence following initial surgery have led the investigators to use different surgical modalities for the treatment of GCT according to stage of the disease aiming at decreasing the rate of local recurrence with good functional and cosmetic results [15–17].

In our case, the tumor had an aggressive type of

evolution and the main risk was represented by the malignant transformation. Diagnosis of transformation relies on overt malignant cytological features, as necrosis and scattered mitoses can be seen in the usual "benign" giant cell tumor of bone. Immunohistochemical studies are not required for the diagnosis of transformation. Usually, there is no evident lineage of maturation, but cases of osteosarcoma have been reported. Given the wide range of reported incidence of malignancy in giant cell tumor of bone among studies, it is probable that this entity has been overdiagnosed in the reported series [18–22].

The giant cell tumor is generally classified as benign but the fast growing rhythm and the aggressive soft tissue invasion demonstrate a malignant potential of the tumor. The main primary treatment of GCT is surgery when an interdisciplinary approach and a very good pre-operative planning are made (plain X-rays, CT/MRI, biopsy). Amputation is preserved for massive recurrences and malignant transformation [23–25].

After we fully diagnosed the nature and the grade of the tumor, the options for the surgical type of treatment were: distal femoral bone resection and replacement with endoprosthesis or allograft, oncological resection with soft tissue and bone reconstruction or even the thigh amputation. Foukas *et al.* [26] reported the use of contained impacted morsellized allograft to revise an aseptically loose, massive distal femoral cemented endoprosthetic replacement and Vicas *et al.* [27] used extensive osteoarticular allografts for knee reconstruction, but because of their composite nature and the technical difficulty of the procedure, complication and failure rates have been very high. Also, the knee joint replacement was not possible because of the associated supracondylar fracture. The fracture compromised the metaphyseal support for the femoral component of the knee prosthesis and the revision component could compromise the local vascularization [28–30].

In our study, the decision regarding the final treatment option was influenced by multiple factors: presence of a supracondylar fracture, young age of the patient and the absence of secondary metastasis.

Conclusions

The follow-up of the presented case demonstrated that using an orthoplastic approach of this patient we manage to remove the tumor within oncological limits and achieved bone healing with good stability of the distal femur. In our case report, we managed to treat a young patient with a pathological fracture of the distal femur. It was an aggressive GCT that invaded the femoral condyles and the adjacent soft tissues. The correct treatment required an interdisciplinary team consisting of orthopedic surgeons, plastic surgeons, pathologists, radiologists and anesthesiologists. The patient underwent three surgeries in 10 weeks, the first one which was the diagnose biopsy and last the third surgery last for over 12 hours. Our results compared with those from literature were very good as there were no complications. The mobility in the knee was kept almost entirely and the patient was able to walk six months after the last surgery. Thus, we managed to restore the local anatomy avoiding serious complications: infection, articular surface collapse or tumor recurrence.

Conflict of interests

The authors declare that they have no conflict of interests.

Acknowledgments

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