GIANT CELL TUMOR OF BONES: MANAGEMENT BY DIFFERENT SURGICAL TECHNIQUES

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ABSTRACT

Objective: To evaluate the clinical outcome of different surgical techniques used in the treatment of giant cell tumor of long bones and their effect on the rate of local recurrence.

Methods: Thirty-seven patients with giant cell tumor of the long bones have been treated between July 1994 and July 2003. All patients were evaluated by clinical examination, plain X-ray, computerized axial tomography and magnetic resonance imaging. Biopsy was taken in all cases to confirm the diagnosis and to define the histological grade of the tumor. Thirty- one patients were treated primarily by curettage and six were treated primarily by wide excision. Selection of the surgical technique was based on site and size of the lesion, soft tissue involvement (intra- or extra-compartmental), tumor grade (histological and radiological) and if recurrent or not. Patients were followed-up for a minimum of two years.

Results: The mean age of our patients at presentation was 29.3 years (ranged from 19 to 52 years) and at last follow up visit 32.1 years (range 24 to 55 years). Seventeen patients were males and twenty were females, (male to female ratio was (1:1.2). According to the classification of Campanacci *et al* (3 patients were grade I, 24 patients were grade II and 10 were grade III). There were no mortalities among our cases. Local recurrence occurred in 9 out of 31 patients treated by curettage.

Conclusion: The main primary treatment of giant cell tumor is surgery. The use of local adjuvant therapy as part of treatment of giant cell tumor helps in decreasing the rate of recurrence. Curettage must be extensive to be effective and requires a large cortical window. Wide excision is used in extremely large lesions with cortical bone breakthrough and extension into soft tissue, when the joint could not be preserved and in cases where resection results in no significant morbidity.

Key words: Adjuvant therapy, Bone cement, Curettage, Giant cell bone tumor, Reconstruction, Resection.

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Introduction

The histogenesis of giant cell tumor (GCT) of the bone is still uncertain. Its histolopathology does not predict the clinical outcome. Many controversies are still present regarding the best method of treatment. Giant cell tumor (GCT) of the bone has been classified by the World Health Organisation (WHO) as "an aggressive, potentially malignant lesion". Almost 75%-80% of GCTs have a benign course. The rate of local recurrence can range from 20% to 50% according to the method of treatment. Malignant transformation at recurrence is not uncommon and reported to happen in about 10% of cases. Approximately 1-4% of giant cell tumors give pulmonary metastases even in cases of benign histopathology.[1-4]

The most accepted hypothesis regarding the pathogenesis of GCT and its neoplastic character is the mononuclear spindle-shaped (fibro-osteoblast like) stromal cells. These cells are genetically

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unstable, and by secreting a lot of cytokines and other factors they stimulate the immigration of blood monocytes into the tumor tissue and promote the formation of the osteoclast - like giant cells. The characteristic cell types, the monocyes and the giant cells, are therefore simply reactive components of GCT, while the spindle shaped stromal cells represent the neoplastic component of the tumor.[5]

GCTs represent 5% of all primary bone tumors and 21% of all benign bone tumors. It has a slight female predominance (1.2 -1.5: 1), and occurs most commonly in the third and fourth decades of life.[6-8] Less than 5% occur in skeletally immature patients.[9] Approximately 50% of GCTs are located about the knee at the distal femur and proximal tibia. Most GCTs are solitary lesions (less than 1% are multicentric).[1,6-8] Pain is the most common presenting symptom, while swelling and deformity are associated with large lesions. The incidence of pathological fracture at presentation is 10-30%.[6-8, 10]

The diagnosis of GCT of bones depends mainly on clinical and radiological examination (plain x-ray, computerized tomography and magnetic resonance imaging) of the site of the lesion. Preoperative biopsy should be taken to confirm the diagnosis and to define the grade of the malignancy.[1,11,12]

The grading system adopted by Campanacci *et al*[7] classifies patients with GCTs, according to their radiological findings, into grade I: means no cortical thinning; Grade II: means some cortical thinning and erosion but no breakthrough; and grade III: means breakingthrough and extension into the soft tissue.

The staging system adopted by Enneking in 1986[12] is also used to stage patients with GCT. It depends on the tumor grade (G), location of the tumor: intra-compartmental or extra- compartmental (T) and presence or absence of metastasis (T).

Surgery is the main treatment of GCTs of long bones with different modalities have been investigated and used.[6-8, 11, 13-18]

GCT is not radio-resistant as it was previously believed. It is reported by many authors that there is local control of 75%-85%.[19- 21]

In this study we describe our nine- year experience with the treatment of GCTs of long bones with different surgical modalities. Attention was directed towards determination of the rate of initial local recurrence, factors that might predispose to recurrence and the results of secondary procedures for the treatment of recurrences.

Methods

Between July 1994 and July 2003, a total of forty-three patients with giant cell tumor (GCT) of the long bones have been treated at the hospitals of the Royal Medical Services (RMS). Of these, Thirty-seven were included in the present study on the basis the documentations available.

All patients were evaluated by clinical examination, routine laboratory tests, local plain X-ray, chest x-ray, computerized tomography and magnetic resonance imaging. Biopsy was taken in all cases to confirm the diagnosis and to define the histological grade of the tumor. The lesions were classified according to the radiographic parameters considered by Campanacci *et al*[7] into grade I, II or III. Different surgical modalities were used including: curettage with bone grafting; curettage with bone cement filling; Curettage and Adjuvant with bone cement and / or Bone graft; wide surgical resection; wide surgical resection with custom- made total joint arthroplasty; wide surgical resection with arthrodesis. Curettage was done through a large cortical window by the manual curette and by the dental burr in some cases. The adjuvant local therapy used in our cases were hydrogen peroxide (H_2O_2) and electrical cautery. Selection of the surgical technique was based on the site and size of the lesion, soft tissue involvement (intra- or extra-compartmental), tumor grade (histological and radiological) and if recurrent or not. Patients were followed-up, clinically and radiologically a minimum of two years (2-9 years) to detect local recurrence, pulmonary metastasis, local complications of surgery and to assess the functional outcomes the patients.

Results

The mean age of our patients at presentation was 29.3 years (ranged from 19 to 52Years) and at last follow up visit 32.1 years (range 24 to 55 years). Seventeen patients were males and twenty were females, (male to female ratio was (1:1.2). According to the classification of Campanacci *et al*,[7] four patients were grade I, 29 patients were stage II and 4 were grade III) Fig. 1. The distribution of the tumor according to the anatomical site showed that approximately 62% of the lesions are located about the knee, at the distal femur and proximal tibia Table I. Three patients had pathological fractures at the time of presentation.

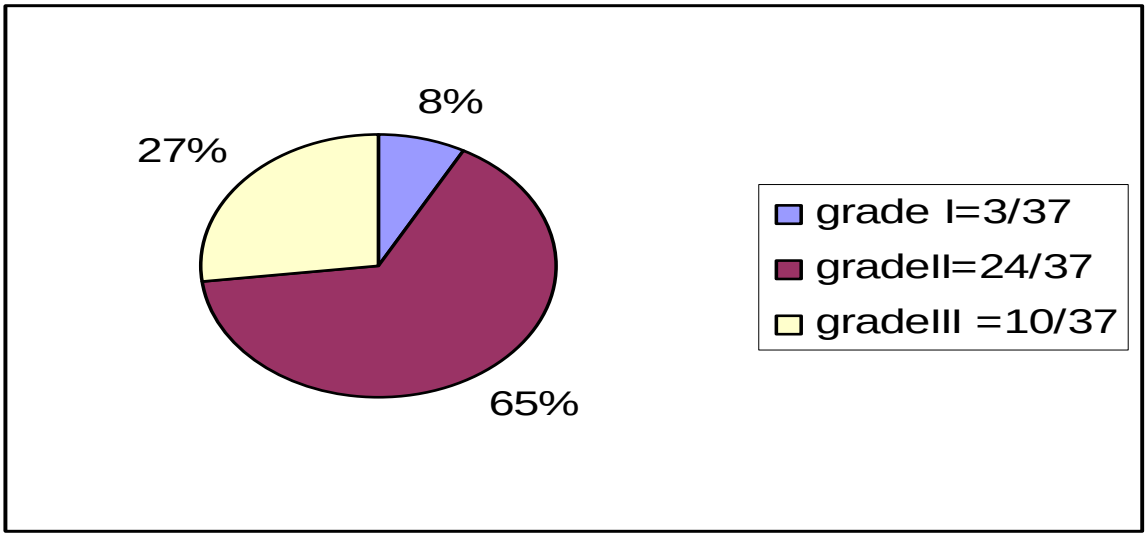

Fig. 1. Distribution of the patients with GCT according to the radiological grade of Campanacci *et al*

Table I. Distribution of GCTs depending on the site

Site of tumor	No. of patients		%	
Distal femur	12	23/37	32	62
Proximal tibia	11		30	
Distal radius	4		10.8	
Proximal humerus	2		5.4	
Distal tibia	2		5.4	
Proximal fibula	2		5.4	
Proximal femur	1		2.7	
Proximal radius	1		2.7	
Distal ulna	1		2.7	
Clavicle	1		2.7	
Total	37		100	

Table II. Distribution of GCT cases according to primary treatment modality

Site of tumor	Curettage + Bone Graft	Curettage + Bone Cement	Curettage+Adjuvant ± bone graft ± Bone Cement	Wide Excision	Wide Excision ± Reconstruction
Distal femur	4	4	4	-	-
Proximal tibia	2	4	5		
Distal radius	3	-	1	-	-
Proximal humerus	-	-	1	-	Hemiarthroplasty 1
Distal tibia	1	-	1	-	-
Proximal fibula	-	-	-	2	-
Proximal femur	-	-	1	-	-
Proximal radius	-	-	-	1	-
Distal ulna	-	-	-	1	-
Clavicle	-	-	-	1	-
Total	10	8	13	5	1

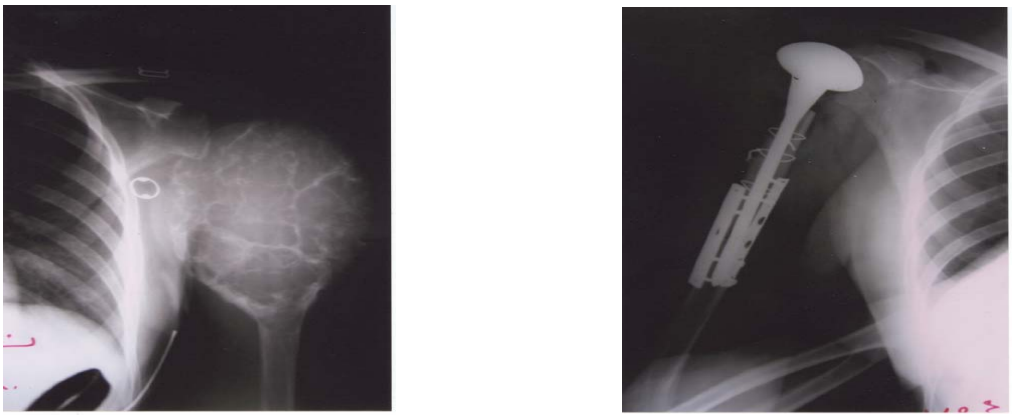

Fig. 2(a,b). GCT affecting the proximal humerus, large in size, causing severe bone destruction (a), treated by shoulder hemi- arthroplasty (b)

Fig. 3(a,b,c). Patient with GCT of the distal femur treated primarily by curettage and bone grafting (a); by curettage and adjuvant therapy with bone cement filling of the cavity for first recurrence (b); and a third surgery of wide resection and reconstruction by an endoprosthesis (custom- made total knee arthroplasty) for the second recurrence (c)

Modalities of primary treatment we used in our patients are shown in Table II. Six lesions were treated by primary wide resection; five of them were present at sites where their removal do not produce significant structural or functional deficit; and one was large in size, causing sever bone destruction and affecting the proximal humerus. This female patient was treated by pre-operative embolization, to decrease the bleeding intra-operatively, and shoulder hemi-arthroplasty Fig. 2. Thirty- one of our patients were treated by curettage using the manual curette and sometime the dental burr. Adjuvant therapy (H_2O_2) was used in thirteen cases. The cavity was filled with autogenous bone graft, bone cement or both.

Nine (24%) of the thirty- seven patients had a local recurrence Table III. All but one recurrence occurred within three years after the primary operation. The majority of recurrences occurred in patients with grade III tumors. The three patients who presented with pathological fracture have developed local recurrence. Patients who got local recurrence have been treated primarily by curettage and bone grafting (6 cases) and curettage and bone cement (3 cases). Lesions managed by curettage and local adjuvant therapy with bone cement and/or bone graft have no recurrences after a minimum follow-up of two years.

All patients with local recurrence, except one, have been treated, secondarily, by curettage (using the burr), adjuvant therapy, bone cement and subchondral bone graft. One patient, with recurrence in the distal radius, was treated by wide excision and a wrist arthrodesis (Case No. 7). This patient developed lung metastasis during follow-up, six months after his second surgery. One patient developed a second recurrence (Case No. 3), with perforation of the articular surface of the distal femur, for which a third surgery of wide resection and reconstruction by an endoprosthesis (custom-made total knee arthroplasty) was done (Fig. 3). This patient got a fracture of his tibia, at the site of the endoprosthesis, which was treated conservatively and

Table III. Data of the patients who had a local recurrence

No.	Age, Sex	Site	Grade	Pathological Fracture	Primary Treatment	Onset of Recurrence (months)
1	F, 19Y	Distal Femur	III	Yes	Curettage + Bone Graft	26
2	F, 27Y	Proximal Tibia	III	No	Curettage +Bone Cement	30
3	M, 33Y	Distal Femur	III	No	Curettage + Bone Graft	12
4	F, 40Y	Distal Radius	III	No	Curettage + Bone Graft	18
5	M,39Y	Distal Tibia	III	No	Curettage + Bone Graft	9
6	M, 34Y	Distal Femur	III	Yes	Curettage + Bone cement	13
7	M,23Y	Distal Radius	III	No	Curettage + Bone Graft	19
8	F, 24Y	Distal Femur	III	Yes	Curettage + Bone Cement	15
9	M51Y	Proximal Tibia	II	No	Curettage + Bone Graft	56

Primary recurrence in case no. 6 has been treated by wide excision and wrist arthrodesis.
Primary recurrences in all other cases have been treated by Curettage +Adjuvant ±Bone graft ± Bone Cement
Case no. 3 developed a second recurrence which was treated by wide excision and a custom- made endoprosthesis (Total Knee Arthroplasty).

healed after 4 months. One patient, with GCT of upper tibia, had rupture of the patellar tendon 4 weeks post-operatively and reconstruction was done. None of our patients died during the follow-up period, and amputation was not done for any.

Discussion

Typically, GCTs occur in the third and fourth decades of life, and the age distribution in our series is consistent with that published in previous reports.[7,8] There were slightly more female patients (54%) than male patients. This finding is also in agreement with some earlier studies, but not with others.[6] The tumor is uncommon in patients with open physis.[7,9] The youngest patient in our series is 19 year old.

Some authors[7,14,17,22] have attempted to correlate the clinical behavior and incidence of recurrence with the initial radiographic grade. Others [15,18,23] found no correlation between the radiographic appearance of the lesions and their clinical behavior. Although statistically insignificant, because of the small number, we observed a strong correlation in our series, especially for lesions of grade III.

Pathological fracture might be the primary presentation in 4%-32% of patients with GCTs. Eckardt[22] treated these cases, in his series, by immediate open biopsy and wide excision. Sung *et al*[6] and Goldenberg *et al*,[8] in two separate studies, have recommended immediate curettage and bone grafting with additional external fixation. Dreinhofer *et al* [10] have treated ten GCTs with fracture at the time of diagnosis by curettage and bone cementing and reported recurrence in two (20%). In our study three patients presented with fracture (8%), one has been treated with curettage and bone grafting and the other two with curettage and bone cementing and all developed local recurrence.

Because GCT is a locally aggressive yet benign disease, intralesional treatment is a limb- sparing option with good outcomes.[1]

Many different methods of treatment of GCTs are reported in the current literature including: curettage; curettage and bone grafting; curettage and insertion of bone cement (polymethylmethacrylate); cryotherapy (liquid nitrogen) after curettage of the cavity; curettage and a chemical or electrical adjuvant (phenol, zinc oxide, alcohol, H_2O_2, argon beam coagulation and electrical cauterization of the inner surface of the cavity) prior to the insertion of bone cement or a bone graft; primary resection; radiotherapy; and embolization of the feeding vessels.[6-8, 13-21]

Although intra-lesional procedures remain the treatment of choice for most GCTs, wide resection offers the lowest recurrence rate (0-20%) and is recommended for lesions in certain locations (proximal fibula, proximal radius, distal ulna, and clavicle) where it leaves no functional deficits.

Table V. The rate of recurrence after different intralesional treatments of primary GCT of bone (minimum follow-up ≥ 2 years)

Author	Number of patients	Adjuvant treatment	Rate of local recurrence
Goldenberg[8]	120	None	43%
Campanacci[7]	128	None	30%
Malawar[13]	102	Burr, Liquid nitrogen	8%
O'Donell[14]	60	Burr, Phenol, Cement	25%
Szendroi[1]	11	Phenol, Cement	9%
Blackley[15]	59	Burr, None	12%
Mcdonald[18]	85	Burr, Phenol, Alcohol	34%
Lausten[24]	18	None, Radiotherapy	56%

Table IV. Recurrence rate in relation to the primary treatment

Primary treatment modality	No. of cases	Number of Recurrence	Recurrence rate
Curettage + Bone Graft	10	6	60%
Curettage + Bone Cement	8	3	38%
Curettage + Adjuvant ± bone graft ± Bone Cement	13	-	-
Wide Excision	5	-	-
Wide Excision ± Reconstruction	1	-	-
Total	37	9	24%

However, in certain sites, wide resection necessitates reconstruction which is associated with considerable surgical and functional morbidity. In our study, none of the seven patients who have been treated by wide excision (6 primarily and one after recurrence) have got recurrence.

Intralesional curettage and bone grafting is a limb-sparing option that is associated with good functional outcomes in most cases. However, simple curettage with or without bone graft has recurrence rate of 27-55%.[7,8,24] Six of the ten patients we have treated by curettage and bone grafting developed local recurrence (60%) Table IV.

The high risk of recurrence led several surgeons to replace bone graft in the lesion with bone cement packing and to investigate different intralesional adjuvant therapies. These presumably remove the tumor cells which remain after curettage because of their thermal or chemical effects.

The data, from literature, summarized in Table V (as presented in the review article of Szendroi[1]) suggest that the use of adjuvants combined with careful curettage may decrease the rate of local recurrence, which were reported in the historical series of Goldenberg *et al* (43%)[8] and Campanacci *et al* (30%),[7] to about 9% in the series of Szendroi.[1] McDonald *et al*[18] found in his big series that the most significant factor in decreasing the rate of recurrence is the surgical procedure employed for removal of the tumor i.e., curettage with adjuvant therapy (34%) versus resection (7%). This result has been confirmed by O'Donell.[14] Bone cement technique, compared with bone grafting, offer the advantages of lack of donor site morbidity, an unlimited supply, immediate structural stability, low cost, easy to use and contains barium that sharply contrast the surrounding bone which makes the local recurrences more readily apparent.

The disadvantages of using cement include difficulty in removing it in revision surgery and possibility that subchondral cement may predispose the joint to early degenerative osteoarthritis. Malawar[13] showed that subchondral bone grafts are superior to cement for restoration of the normal subchondral anatomy. We have used curettage and cement in the treatment of eight patients with 3 recurrences (38%).

Several authors have added the technique of high speed burring of the cavity after simple intralesional curettage. A large cortical window is necessary to expose the entire tumor cavity. O'Donnell[14] and Blackley,[15] found this technique efficient to decrease the rate of local recurrence to 12%, 17% respectively.

Adjuvant therapies have advantages and disadvantages. However, they all offer a method for eradication of microscopic tumor tissue. Recurrence rates with curettage and phenol 5% and packing with bone cement or bone grafts are 5-17%.[14] Blackley[15] have raised the concern of the rapid phenol absorption through cancellous bone and its hazardous effect on the CNS, heart, kidney and liver.

Many authors[11,13,17] advocated cryosurgery (liquid nitrogen) as an adjuvant. They reported 2-12% recurrence rate. Fracture was the most commonly reported complication. Malawer[13] suggested that all

patients who undergo cryosurgery should receive internal stabilization as well.

We did not use phenol, cryosurgery, argon beam, zinc oxide or alcohol in any of our cases. Curettage followed by high speed burring and H_2O_2 lavage with bone cement filling with or without subchondral bone graft was used in 14 patients (13 primary and one recurrent), One of them developed recurrence (7%).

The management of local recurrence of GCT varies. Some authors,[7,22,24] recommend wide excision for any recurrent lesion, where as others[10,16,17] believe that rpeated intralesional surgery with adjuvant for the second or third recurrence is justified. We repeated the intralesional surgery for all except one of our patients.

Many authors[19-21] recommend megavoltage radiation as a reasonable alternative to complex and difficult surgery, especially in areas where surgery is not accessible or in patients with high risk for surgery .None of our patients have been treated by this method.

Approximately three percent of GCTs metastasize to the lung.[3,4] This complication occurred in one of our cases. One of our patients with a GCT in the proximal tibia has got a rupture of his patellar tendon which was reconstructed. Another female patient presented with a subcutaneous soft tissue nodule with a calcified rim at the scar of the previous surgery.

There were few patients in each subcategory for us to demonstrate statistical significance, but the rate of local recurrence seemed to be higher in patients who had a tumor of the distal radius, those who had an associated pathological fracture, and those who had a grade- III lesion according to the classification of Campanacci *et al.*[7] Use of high speed burr and adjuvant local therapy may have decreased the rate of local recurrence.[15,23] Functional outcomes and patients satisfactions were good to excellent, which were similar to those of many authors.[23, 25-27]

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