

# **GAIN T CELL TUMOR OF BONES EVALUATION AND TREATMENT**

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## **INTRODUCTION**

Giant cell tumor of bone is a benign but locally aggressive and destructive lesion with a tendency for local recurrence. Nomenclature has changed over the years. Various names have been suggested and adopted since 1818, till date like: Myeloid leukemia, Myeloid tumor, Tumor of Myeloplexus, Osteoblastoclastoma and finally Giant cell tumor<sup>3</sup>. GCT also has a tendency to develop benign pulmonary metastatic implants in a small percentage of cases which has caused considerable debate over the exact nature of lesion<sup>10,27</sup>. As per reports from Asian literature it accounts for 20% of primary skeletal neoplasms in oriental countries.<sup>5,15,29</sup> It generally occurs in skeletally mature individuals with its peak incidence in third decade of life with slight female predominance (1-1.3)<sup>4,7,10,28</sup>. The most common sights include distal femur, proximal tibia and distal radius.<sup>4,28</sup> GCT typically involves the epiphysiometaphyseal region of long bones.<sup>14,26</sup> Histologically the lesion is composed of osteoclast like multinucleated giant cells in a moderately vascularised network of proliferating round, oval or spindle shaped stromal cells.<sup>30</sup> MRI is currently the best imaging modality for GCT and is useful in determining extraosseous extend and articular surface involvement.<sup>18</sup> Owing to continued progress and development in the field of orthopaedic oncology, the concept of limb salvage has now become established for locally advanced, aggressive, benign and even some contained malignant bone tumors. Enneking and Campanicci's radiologic classification and surgical staging are helpful in planning the initial surgical treatment. Small and localized tumors (Stage I and in some cases Stage II) respond well to procedures like intralesional curettage with bone graft<sup>6,10</sup>/bone cement<sup>17,23</sup>/cryosurgery. While advanced / recurrent tumors require more radical surgery (excision / en-bloc resection followed by reconstructive procedures)<sup>2,25,33,34,35</sup>.

## **MATERIAL AND METHODS**

25 cases of established giant cell tumor of bone between Jan 1998 to July 2003 were studied. Patients of all age groups and both sexes were included in the study. Each case was subjected to complete workup which included clinical examination, routine investigations, X-rays (local and chest), CT and MRI wherever indicated. Bone scan and open biopsy was done in all cases. To know the histological staging and to define surgical margin, Enneking classification system was used. Radiological evaluation was based on Campanicci classification.

### **Enneking's Classification**

- I. Benign Lesions: Encapsulated, intracompartmental, cell to matrix ratio is low, no hyperchromasia or anaplasia.
- II. Active Lesions: Can expand by deformation of overlying cortical bone, cell to matrix ratio is relatively balanced, remain encapsulated.

- III. Aggressive Lesions: Readily penetrates the natural barriers to tumor growth, high cell to matrix ratio, frequent hyperchromatic nuclei, pathological fracture may be seen.

#### **Campanicci's Classification:**

- I. Quiescent: Cortical bone is slightly thinned and not expanded.
- II. Active: The cortex is very thinned, at time it is nearly cancelled but tumor is clearly bordered by periosteum.
- III. Aggressive: Cortex appears to be cancelled, with expansion towards the soft tissues of a globose tumor having no radio opacity.

After histopathological confirmation various surgical treatment modalities were offered. Patients were operated under regional/general anaesthesia. Tourniquet was used in those cases where surgical margins permitted its use. Biopsy scar mark was incorporated within incision at time of surgery and was excised along with tumor. Following surgical procedures were offered:

1. Curettage and bone grafting: Ten patients were treated with curettage and bone grafting. Extended curettage was done using high speed burr and cavity was washed three times with 40% phenol alternating with normal saline. Type of bone graft was decided on basis of site of lesion, extent of lesion and availability of autograft. Donor sites were Iliac crests and fibulae.
2. Curettage and Bone Cementing: Two patients were treated with curettage and bone cementing. This procedure was done in lesions more than 5 mm away from articular surface.
3. En-bloc resection: This was done in two patients, one patient with GCT of proximal fibula and one of distal ulna where resection of lesion with bone does not leads to any functional disability.
4. En-bloc resection + arthrodesis: This was offered in one case involving proximal tibia with intraarticular extension. Fibular strut grafts were used and internal fixation was done with long plate.
5. En-bloc resection + fibular arthroplasty: This procedure was offered to all the five cases with GCT distal end radius. Fibular grafts were taken from ipsilateral side. The grafts were fixed using DCP and additional stability was provided by using two K-wires – one placed transversely just proximal to wrist joint from ulna to radius and another passing from radius to third metacarpal.
6. En-bloc resection + prosthetic replacement: This was done in one case of GCT proximal humerus (Neer's prosthesis) and one case of distal humerus (elbow prosthesis).
7. Amputation: Primarily two above knee and one below elbow amputations were done as tumors were infected and fungating.

Resected and curetted tumor tissue were sent for histopathological examination.

#### **Post-operative**

POP slab was applied in all the cases except where amputations were done and in one case where Neer's prosthesis was used. Immobilisation in cast was done after stitch removal and was continued upto six months in cases treated with curettage and bone grafting, arthrodesis and fibular arthroplasty. In cases of lower limb, partial weight

bearing was started when adequate healing was observed on X-rays and use of a brace was continued till grafts were fully incorporated.

**Follow up**

All cases were followed up postoperatively by serial local X-rays and X-rays of chest once every month for three months, then every three months upto a minimum period of one year. The cases were followed up radiologically and clinically to see any local and distant recurrence of tumor, signs of union, graft uptake, implant loosening, any signs of infection or any other complication. Cases where recurrence was suspected, FNAC/Biopsy was done to confirm the diagnosis.

**OUTCOME**

Functional assessment at last follow up was done on basis of Musculo Skeletal Tumor Society (MSTS) criteria which takes into consideration the following points:

- For either extremity:- Pain, Function, Emotional acceptance
- For lower extremity:- Supports, Walking ability, Gait
- For Upper Extremity:- Hand positioning, Manual dexterity, Lifting ability

The results were assigned as Excellent (>85% of normal function)

Good (70%-84%)

Fair (55%-69%)

Poor (<55%)

**Overall result (lower limb)**

Result	No of patients
Excellent	5
Good	4
Fair	4
Poor	1
Total	14

**Overall result (upper limb)**

Result	No of patients
Excellent	6
Good	3
Fair	0
Poor	2
Total	11

## **Oncological results**

Local recurrence was found in a total of 5 patients within a period of 2 years. Earliest recurrence was noticed at 8<sup>th</sup> month. In three patients (60%) site of recurrence was proximal tibia. One recurrence each occurred at distal femur and distal tibial level. All these patients were treated with curettage and bone grafting primarily. All the recurrences were observed in Campanicci grade II tumors.

## **ANALYSIS**

Of the 25 patients male comprised 52% (13) while 48% (12) were females. 40% (10) of the patients were in their 3<sup>rd</sup> decade of life, 24% (6) were in 4<sup>th</sup> decade, 20% (5) in 2<sup>nd</sup> decade, 8% (2) in 5<sup>th</sup> decade, 4% (1) each in 7<sup>th</sup> and 8<sup>th</sup> decades.

The maximum number of lesions were around knee (upper end tibia and lower end femur) i.e. 12 (48%). This was followed by distal end radius 6 (24%). Two lesions (8%) were present in distal end humerus. 1 (4%) each in distal end tibia, proximal end humerus, distal end ulna, proximal end fibula and proximal phalanx little finger. Pain was presenting symptom in 15 cases (60%), 6 patients (24%) presented with pain and swelling. 4 patients (10%) presented with only swelling. The average duration of symptoms at time of presentation was 5.2 months. 20 (80%) of patients presented within 6 months of appearance of symptoms.

17 (68%) cases presented with histological grade II lesion on the basis of Enneking classification with epiphysiometaphyseal region being the commonest location along longitudinal axis (92%). 21 patients (84%) had subchondral extension out of which 17 (68%) patients had extension within 1 cm of subchondral cortex and 4 patients (16%) had lesion more than 1 cm from subchondral cortex. Intraarticular extension was seen in 4 patients (16%).

Curettage and cancellous bone grafting was done in 10 cases – proximal tibia (4 cases), distal femur (3 cases), distal tibia, distal humerus and proximal phalanx (1 each). Along with cancellous graft, fibular graft was used in 3 patients – proximal tibia, distal femur and distal humerus. Along with bone graft, fixation (screws) was used in one case of distal humerus. 2 patients (8%) were treated by curettage and bone cementing. One tumor each was present in proximal end tibia and distal end femur. En-bloc resection was done in 2 cases (8%) – 1 tumor each was present in proximal end fibula and distal end ulna. En-bloc resection and fibular arthroplasty – 5 cases (20%), En-bloc resection and arthrodesis – 1 case. Amputation – 3 cases (12%), En-bloc resection and prosthetic replacement – 2 cases (8%). Minimum follow up period was 1 year with 64% of patients having a follow up of > 2 years. The average period of incorporation of graft/radiological union was 10.3 months (both upper and lower limbs). Full weight bearing was started within a week of suture removal in 3 patients, at 8 to 10 months – 4 patients, 10 to 12 months – 3 patients, >12 months – 2 patients. There were three complications:- Wound infection (1 case), Shortening of lower limb by 10 cm (1 case), Fibular graft fracture and pulmonary metastasis (1 case) 5 patients (20%) developed recurrence within a period of 2 years. In 3 patients site of recurrence was proximal tibia and one each at distal femur and distal tibia.

## **DISCUSSION**

Most patients incurring a giant cell tumor of bone are young and active with normal life expectancy. The aim of treatment is to remove the tumor completely and to preserve the joint. These aims have not changed, but the approach and results of

treatment have changed with time. Although more commonly reported in females, in our study the tumor was found commonly in males (52%)<sup>1,32</sup>. Most lesions are located about knee<sup>4,10,14,29</sup>. In our series, 48% of giant cell tumors were in distal femur and proximal tibia. Distal end radius was the second most common location. In 96% of patients, the lesion was primarily in epiphysiometaphyseal region and only 4% of lesions occurred in metaphyses without involvement of epiphyses. Other authors<sup>10,14</sup> found involvement of epiphysiometaphyseal region between 98-99%. GCT are considered benign lesions but local recurrence rates can be high and several surgical approaches have been advocated in an effort to minimize this risk. Simple curettage yields recurrence rates between 27% and 55%, regardless of whether or not bone graft is used to fill the defect<sup>19</sup>. Patients treated with bone grafts often require prolonged protected weight bearing until graft incorporation. So we have used curettage along with bone grafting in stage I and stage II cases and that too with local cytotoxic agent (Phenol). McDonald<sup>19</sup> has found phenol to reduce recurrence rate from 50% to 35%. Autogenous grafts have the advantage of restoring normal bone integrity after grafts have healed and joint motion and function is preserved. Acrylic cement enhances the margin of tumor cavity by 1.5 to 2 mm in cancellous and 0.5 mm in cortical bone.<sup>20,24</sup> Because the cement filled defect is mechanically stable, patients can bear weight immediately and rehabilitate quickly. Reduced recurrence rates have been reported using acrylic cement (between 3% and 15%)<sup>8,24</sup>. Another benefit of using acrylic cement is that recurrences are readily discernible at the bone-cement surface.

In some stage II and all stage III cases we have used more radical surgeries. En-bloc resection is suggested to be a easier therapeutic choice for giant cell tumor occurring in expendable bones such as proximal fibula and distal ulna<sup>14,18</sup> without any gross disability. En-bloc resection and fibular arthroplasty is considered as treatment of choice for lesions present at distal end radius<sup>9</sup> as it is aggressive and rapidly growing in this region. In the present study we treated all these 5 patients with En-bloc resection and fibular arthroplasty. En-bloc resection and arthrodesis is suggested if tumor involves proximal tibia because of problems arising from resection of patellar tendon.<sup>13</sup> One patient in our series with grade III tumor of proximal tibia received similar treatment using fibular graft and fixation with long plate. Such patients had a more stable limb and performed most demanding physical work.<sup>12</sup> Amputation as primary mode of treatment has been advocated by various authors,<sup>4,14,29,32</sup> when there is extensive bone destruction with soft tissue extension, severe disability, infection and malignant transformation. Two patients in this series underwent above knee amputation and 1 patient received below elbow amputation for GCT distal radius. Although use of endoprosthesis following En-bloc resection requires function restriction and prolonged bracing<sup>18</sup>, we used Neers prosthesis and elbow prosthesis in two cases with lesions involving proximal humerus and distal humerus respectively as the patients had not much physical demands and could afford the cost of prosthesis.

The average follow up period was 2.7 years and all the patients were alive and mobile at the time of last follow up. Radiological union/incorporation of graft took an average period of 9.5 months in lower limb which was somewhat early as compared to upper limb where average period was 11.2 months. Consolidation at host graft junction occurs earlier when patient is permitted to walk in protective cast after signs of early union.<sup>35</sup> Full weight bearing was usually allowed gradually within one month of partial weight bearing or when well tolerated by patient. In 2 patients full weight bearing was

delayed beyond 12 months as one of them had undergone En-bloc resection and arthrodesis of knee, while other patient showed delayed graft union.

Recurrence is a well known complication associated with GCT of bones and usually occurs between 2-3 years.<sup>4,14,29</sup> All the recurrences in our series i.e. 5 cases occurred within two years, were grade II histologically and had been treated by curettage and bone grafting. Grade II tumors have highest rate of recurrence<sup>22</sup> as grade I tumors are benign and grade III tumors are treated more aggressively. In present series, recurrence rate following curettage and bone grafting was 20% when followed up for 1 year and it increased to 50% when followed up for 2 years. No further recurrence was seen. In view of high recurrence rate (50% treated with curettage and bone grafting) in this series, it may be surmised that curettage alone should be preserved only for those cases when the patient does not agree for more radical surgery and risk of recurrence must be explained to the patient. One case in our study had recurrence with malignant transformation. This has been described as “Evolutionary Malignant Giant Cell Tumor”.<sup>7</sup> No recurrences were seen in patients treated with curettage and bone cementing<sup>4</sup>, En-bloc resection and Amputation. More aggressive treatment has been suggested by some authors in case of recurrent tumors<sup>11,24</sup> and on the other hand Douglas et al<sup>10</sup> described that recurrent lesions probably do not represent biological aggressiveness and that a second or even third less radical operation with or without adjuvant therapy such as acrylic cement or bone graft placed in cavity is justified. We treated two patients with curettage and bone cementing following recurrence. The lesions were one each at proximal tibia and distal femur. Curettage and bone grafting was repeated in one patient with recurrence at proximal tibia as the lesion was within 1 cm of subchondral bone. Above knee amputation was done in one patient who had recurrence with malignant transformation at proximal tibial level. Excision arthrodesis was done in 1 patient who had recurrence with intraarticular extension at distal tibial level.

Wound infection was found in one patient who was treated with curettage and bone cementing at proximal tibial level which was dealt by debridment and antibiotics. Shortening of lower limb by 10 cm was seen in 1 patient following En-bloc resection and arthrodesis of knee and was treated using Ilizarov’s technique. At last follow up there was limb length discrepancy of 2 cm. Primarily treating giant cell tumors of proximal tibia using Ilizarov’s method after tumor resection have shown excellent results.<sup>31</sup> Fibular graft fracture three years after surgery was seen in one case who had undergone fibular arthroplasty for lesion at distal end radius and fracture was fixed by replating and bone grafting which is considered as an ideal option.<sup>21</sup> Radiological union occurred at 10 months. The same patient was detected having solitary pulmonary metastasis. Approximately 3% of GCTs metastasise to lung<sup>16,27</sup>. The patient refused for surgical resection of pulmonary lesion which is suggested as treatment of choice when possible.<sup>14</sup>

All the patients were assessed for functional outcome at last follow up according to MSTS criteria. 21 patients (84%) were pain free whereas 4 patients (16%) had modest/ non-disabling pain. Out of a total of 14 patients who were operated upon lower limb, 12 patients (85.7%) were walking without support. On comparing the functional ability of patients who had undergone excision arthrodesis with those who were using artificial limbs following amputation, had a more stable limb and performed most demanding physical work. Amputees had difficulty walking on steep and rough surfaces

but were least worried about damaging the affected limb. Amongst patients operated upon lower limb, 5 patients (35.7%) had excellent results, 4 patients (28.5%) showed good results and 1 patient (4%) had a poor result. Upper limb surgeries were performed on 11 patients and 9 patients (81.8%) had unlimited hand positioning with overall excellent results in 6 cases (54.5%). 3 patients (27.2%) had good results and poor results were seen in 2 (18.1%) patients. Patients who had undergone En-bloc resection or prosthetic replacements had no or very little restrictions in activity and were more than satisfied or enthused with the results. Same was true for 3 out of 5 patients who had undergone resection and fibular arthroplasty for lesions involving distal end radius. Patients treated by curettage and bone grafting had overall good results, whereas excellent results were found in 2 patients treated with curettage and bone cementing.

## **CONCLUSION**

GCT is one of the unpredictable lesions of orthopaedics and it presents in different grades of aggressiveness. From review of literature and from present study it is clear that the consistently accurate prediction as to local recurrence or pulmonary metastasis could not be made on basis of histological grading. There is a high recurrence rate following curettage + bone grafting. Cases treated by curettage + bone grafting should be followed more regularly as incidence of recurrence increases with time. En-bloc resection in all grades has stood the test of time and probably is the best form of treatment. Custom made prosthesis is a successful alternative in defect reconstruction, but its role in young patients is limited and the cost takes beyond reach of ordinary Indian patients. Arthrodesis of adjacent joint is a small price to pay for resolution of original problem when the result is a stable extremity without local recurrence and when arthroplasty is not possible due to financial problem and/or age. Primary amputation is not desirable and is indicated only when limb salvage is not possible.

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