Reducing Recurrence in Campanacci Type Three Giant Cell Tumor of Bone: Outcomes from an 82-Case Study Evaluating Psuedocapsule Excision with Extended Curettage

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ABSTRACT

Background & Objective: In Campanacci type 3 giant cell tumor of bone (GCT), soft tissue expansion of the tumor has been considered the most important factor for recurrence. We report the outcomes in 82 consecutive patients with GCT of the extremities treated with the excision of pseudocapsule along with extended curettage in terms of recurrence and functional results. **Material and Methods:** We treated 82 cases with histologically proven, radiological grade 3 GCT of the extremities, which had at least two cortices intact. We performed soft tissue expansion excision along with extended curettage using a high-speed burr, phenol, hydrogen peroxide, and electrocautery. Reconstruction was done with bone cement or bone graft, and internal fixation was performed in all cases. Cases were followed up for a minimum of two years. **Results:** The highest incidence of GCT was found in the distal femur (28 , 34.1%), followed by the proximal tibia (18, 21.9%), with the third most common sites being in the upper limb, where the distal radius and proximal humerus each had an equal incidence of 12 cases (14.6%). Eight patients had preoperative pathological fractures. Reconstruction with bone cement was done in 65 cases, and bone grafting was done in 17 cases. Recurrence of GCT was not observed in study population. Post-operative infections were seen in 2 patients. **Conclusion:** Soft tissue expansion and pseudocapsule excision along with extended curettage are effective methods for decreasing the rate of recurrence in giant cell tumors of bone.

Keywords: Giant cell tumor, Campanacci type 3, Pseudocapsule, Recurrence.

INTRODUCTION

Locally aggressive, generally benign, giant cell tumors are one of the most common benign bone lesions, accounting for approximately 5-7% of all bone tumors and 20% of benign bone tumors.[1, 2] These neoplasms commonly occur in young adults, mostly in the third decade of life, within the age group of 20-40 years, with a female predominance.[3] They are epiphyseal or meta-epiphyseal tumors, with 60% of them affecting the bones around the knee joint.[4,5] Although benign, malignant transformation can occur in about 1% of these neoplasms, with pulmonary metastasis reported in about 1-6%.[5]

The management of these lesions poses a challenge to treating surgeons due to a high incidence of recurrence post-intervention, with no one method established as superior to the others. Various surgical options are available, including simple curettage with bone grafting/bone substitution, segmental resection, extended intralesional curettage with a high-speed burr, phenolization, and a variety of other options, including cryosurgery,

radiotherapy, and embolization of feeding vessels.[6] Campanacci et al. classified GCTB into three grades: grade 1 - a static form with minimal involvement of the cortex; grade 2 in which the cortex is thinned and expanded, and grade 3 in which the lesion penetrates the cortex and has a soft tissue expansion. In Campanacci type 3 GCT, soft tissue expansion of the tumor has been considered the most important factor for recurrence. I It becomes difficult to curette these soft tissue expansions with mechanical methods due to their proximity to vessels, making it onerous for the application of chemical and thermal agents.[7]. We hypothesize that meticulous excision of soft tissue expansion and resulting pseudocapsule (marginal excision) along with extended curettage on bony surfaces should result in decreased incidences of recurrence.

The present study aims to establish the efficacy, in terms of oncological and functional outcomes, of extended curettage with marginal excision and high-speed burring of the cavity in the Indian setting for patients with Campanacci grade 3 GCT.

MATERIAL AND METHODS

A prospective interventional descriptive study was conducted at a tertiary-level medical college attached hospital between April 2015 and May 2022. Approval from the Institutional Ethics Committee was obtained before commencing the study (IEC NO. 1124/MC/EC/2015).

All patients presenting to the Outpatient Department of our hospital suspected of having a Giant cell tumor of extremities based on imaging (X-ray, CT scan, MRI) underwent radiological and clinical staging and were subjected to image-guided core needle biopsy of the lesion. The study included histologically proven, operable Giant cell tumors with a radiological grade 3 according to Campanacci classification with at least two cortices intact. Patients previously treated with Denosumab, those with localized infections due to previous surgery, and those with neurological deficits were excluded from the study. Written informed consent from all patients was obtained prior to inclusion in study.

All participating patients underwent extended intralesional curettage after creating a wide bone window in the tumor cavity without opening the joint capsule. Surrounding tissues were protected from tumor spillage or implantation using a solution of wet hydrogen peroxide (50%) and normal saline mops. The tumor was thoroughly scraped using bone curettes, and bone ridges were ground with high-speed burrs, with the range of grinding varying from 1 mm to 10 mm. The cavity was then rinsed with saline, and the cavity wall was cauterized until it turned black, after which the blackened surface was scraped again. Subsequently, a 10% phenol coating was applied over the cavity wall, followed by another rinse with saline. After curetting the cavity, excision of the surrounding pseudo-capsule and reactive tissue zone around the cavity was performed. This procedure was referred to as marginal excision. A pre-contoured locking compression plate was applied with diaphyseal screws. The length of metaphyseal screws was measured and kept ready to be applied after cement application. The cavity was filled with PMMA bone cement, and during the doughy phase, plate fixation was completed by applying pre-measured metaphyseal screws to provide stability. After the bone cement had settled, the cavity was again washed with hydrogen peroxide and saline. Overlying soft tissue was approximated, and the skin was closed using 2-0 Nylon interrupted sutures. For the medial condyle of the tibia, a gastrocnemius flap was routinely employed. In cases where the GCT was located in the proximal femur, and the cavity was small, structural integrity remained intact after curettage, and there was an absence of pathological fracture or involvement of only one cortex, iliac crest bone grafting was used to fill the cavity instead of bone cement, followed by plate or nail fixation. All procedures were performed by a single surgical team to standardize the results. Patients had a postoperative stay ranging from 3 to 5 days. In patients where bone cement was used as a cavity filler, joint mobilization exercises and full weight bearing with support were started from the second postoperative day or based on the patient's pain tolerance. In patients where iliac crest bone graft was used, partial weight bearing protocol was employed for 3 to 6 weeks, after which gradual full weight bearing was allowed.

All patients were followed up at 2 weeks for suture removal, and then every three months for the first year, and once every six months in the second year. Subsequently, they had been undergoing annual follow-ups till last reporting. At each follow-up, patients were clinically assessed for recurrence of pain or swelling, and X-rays of the affected extremity were taken to assess the appearance of any new lytic areas or loosening of implants and cement. Functional scores were assessed using the Musculoskeletal Tumor Society Score (MSTS)[8] at the last follow-up. Chest X-rays were also ordered to rule out metastasis. All patients were followed up for a minimum of 2 years.

Statistical analysis: After inputting the data into a spreadsheet using Microsoft Excel, statistical analysis was performed using the statistical application SPSS version 21.0. Quantitative variables (numerical variables) were presented as the mean and standard deviation, while qualitative variables (categorical variables) were presented as frequencies and percentages for each category. Appropriate statistical tests, such as t-tests, were used based on the specific data distribution and research question. *P* -value less than 0.05 was considered statistically significant.

RESULTS

A total of 82 patients were enrolled in the present study (April 2015-March 2020), of which 36 were men and 46 were women. The mean age of the patients in our study was 25, ranging from 15 to 54 years. Out of the 82 patients, 77 (93%) underwent treatment for a primary lesion, while 5 (6%) were treated for recurrences. All enrolled patients were histologically confirmed to have a radiological grade 3 Campanacci giant cell tumor of bone. The most common location for GCT was the distal femur (28, 34.12%), followed by proximal tibia (18, 21.95%), proximal humerus (12, 14.63%) and distal radius (12, 14.63%) (Table 1). Among these, 5 were recurrent lesions, including 3 lesions in the distal femur, 1 lesion each in the proximal tibia and distal radius.

Table 1. Distribution of cases of Campannaci grade 3 Giant cell tumour according to the bone involved

Bone involved	Number	Percentage (%)
Distal Femur	28	34.14
Proximal Tibia	18	21.95
Proximal humerus	12	14.63
Distal radius	12	14.63
Proximal femur	9	10.97
Distal humerus	2	2.43
calcaneum	1	1.21
Total	82	100

Eight (9.75%) of our patients suffered pre-operative pathological fractures, with seven occurring in patients treated for GCTs of the distal femur (figure 1), and one in a patient treated for proximal femur GCT. Post-operative infections were observed in 2 patients of medial condyle proximal tibia GCT within two weeks of index surgery. These patients were managed with the removal of infected implant and bone cement, followed by the reapplication of antibiotic-impregnated bone cement and a gastrocnemius myofascial flap. Infection in these cases had healed at the final follow-up.

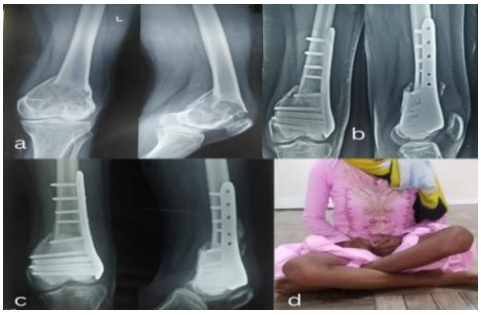

Fig. 1 Radiographs showing Campanacci type 3 GCT of left side distal femur with pathological fracture in a 28 year old female. (a) Pre-operative X-ray, (b &c) Post operative X-ray at 1 month and 36 months, (e) functional recovery at final follow up.

Mean follow up was 53.85 months out of which 38 patients has completed follow up of 5 years or more. Two out of 82 patients (2.43%) presented with recurrence of pain, swelling and lytic lesions around the bone cement on radiological investigations after 6 months and one year from the index surgery. In both of these cases, the recurrence of symptoms was associated with a new malignant neoplasm, as demonstrated in repeat biopsies. One patient was diagnosed with osteosarcoma, and other patient was diagnosed with synovial sarcoma. Both patients were managed with amputation and adjuvant chemotherapy, but the patient with synovial sarcoma succumbed to multiple metastases after 6 months. In the latest follow-up, except for these two cases, all other patients had a satisfactory functional limb with no recurrences or pulmonary metastases.

Reconstruction in our series was done by plate or intramedullary nail fixation along with either bone cement or bone grafting, with PMMA bone cement being the preferred option used in 65 (79.26%) cases (figure 2) and bone grafting being used in only 17 (5 distal femur and 3 proximal tibia) out of the total 82 cases. All proximal femur (n=9) cases were treated with bone grafting. Functional status was assessed using the MSTS score at annual follow-ups, and at the end of two years follow-up MSTS score was compared to each patient's preoperative status. Mean preoperative MSTS score was 34% (ranging from 7% to 50%) and mean postoperative MSTS score was 77% (ranging from 54% to 94%). The difference between preoperative and postoperative MSTS functional scores was found to be significant (Tables 2, 3) at the end of 2 year follow-up.

Table 2. Paired t-test MSTS Score

		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	Preoperative	10.213	80	4.0368	0.4513
	Postoperative	23.33	80	2.633	0.294

Table 3. Paired Samples Test

Pair 1	Paired Differences					t	df	Sig. (2-tailed)
	Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference				
				Lower	Upper			
Preoperative - Postoperative	-13.1125	4.7119	0.5268	-14.1611	-12.0639	-24.890	79	0.000

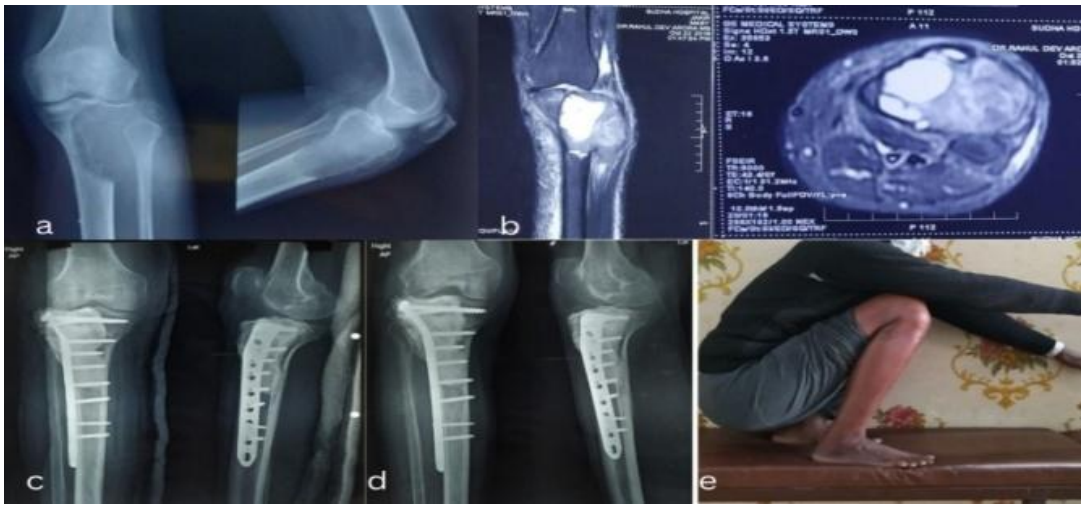

Fig. 2 Radiographs showing Campanacci type 3 GCT of right-side proximal tibia in a 37-year-old male. (a) Pre-operative X-ray, (b) Pre operative MRI, (c &d) Post operative X-ray at 1 month and 24 months , (e) functional recovery at final follow up.

DISCUSSION

Giant cell tumors are unique in their own right. They occur mostly between the ages of 20 and 50 years, with a peak incidence observed in the third decade of life. In our study, the mean age of the patients was 25, ranging from 15 to 54 years, which is consistent with various other studies.[3,4,5] GCT shows a slight predominance in female patients. The female-to-male ratio in GCT varies across different studies and populations but often falls within a range of 1.2:1 to 1.5:1.[3,4,7,9] Our study also supports this observation. In our study, out of 82 patients, 46 were women and 36 were men, with a ratio of 1.27:1.

Their peculiar location and locally invasive nature make their management a challenge for treating surgeons. These tumors have a propensity to involve bones along the knee joint. The maximum incidence of GCTs in our study was found in the distal femur, with 28 cases (34.1%), followed by the proximal tibia with 18 cases (21.9%). The third most common sites were in the upper limb, with the distal radius and proximal humerus each having 12 cases, accounting for 14.6% each . These results were consistent with various studies in the literature, which have reported that almost 50-60% of GCT cases affect the bones around the knee joint, including studies by Balke et al [4] and Blackley et al [5] among many others.

These tumors grow expansively and can easily penetrate the cortex of the bone, sometimes causing pathological fractures[9,10] . Although they rarely invade the joint capsule, these tumors can invade the subchondral bone and destabilize the joint. This has important implications, especially in weight-bearing joints like the knee, as it can lead to debilitating functional morbidity[6,11].

A wide spectrum of treatment options is available for management of these tumors. These options range from simple intralesional curettage, extended curettage using a high-speed burr, to adjuvant treatments like application of liquid nitrogen, phenol, electrical cauterization, and finally, wide excision, either by segmental resection or amputation.[4-6] Simple intralesional curettage leaves the patient with almost normal limb function but has limited efficacy due to high recurrence rates, which range from 30-60%.[4,12,13] However, these rates can be reduced to 6-25% with the application of adjuvants and high-speed burr drilling of the tumor wall[14]. Due to the high cost, high infection rate, need for multiple revisions, and significant functional morbidity associated with wide excision and endoprosthetic reconstruction, its use is limited in the young population.[15] Wang et al[15] and Asavamongkolkul et al.[16] reported no statistically significant difference in local recurrence between extended intralesional curettage and wide excision for grade 3 GCTs. However, these results were questioned in studies conducted by Lopez-Pousa et al.[17] in 2015, who

reported a 20-56% incidence of recurrence even after the use of adjuvants, and many other studies reporting a recurrence rate of more than 20%[4,18]. Heidjen et al.[7], in their retrospective study on 93 patients with GCTs affecting long bones, suggested that the most important factor for local recurrence was the soft tissue expansion of the tumor, which leads to the formation of the reactive zone/pseudocapsule of the tumor. This zone consists of a discoloured area around the tumor, comprising hemorrhagic tissue, degenerated muscle, and edema. Increased technical difficulty in curettage by mechanical methods at the pseudocapsule site and the lack of adequate adjuvant therapy application in the presence of soft tissue expansion are primarily responsible for increased recurrence rates.[19] This is supported by Balke et al.[4] in their study of 214 cases of Giant cell tumors treated with extended curettage, where grade 3 Campanacci tumors showed a staggering 36% recurrence post-treatment.

The aim of the present study was to determine whether extended curettage, along with marginal excision of the pseudocapsule for grade 3 Campanacci GCTs, provides us with an optimal treatment modality that not only reduces recurrences to a minimum but also leaves our young patients with a functionally normal joint and limb.

We treated our patients by performing a marginal excision of the surrounding pseudocapsule of the tumor after extended intralesional curettage using a high-speed burr, electrocauterization and local application of 10% phenol on the remaining tumor cavity wall. Recurrence of symptoms, such as pain and swelling, was noted in only 2 out of the 82 patients (2.43%) enrolled in our study at 24 months of follow-up. In both of these cases, a secondary malignancy was diagnosed on a second biopsy, with osteosarcoma and synovial cell sarcoma being the lesions diagnosed on recurrence. No recurrence of a giant cell tumor was reported in the present study. This supports the findings of Heidjen et al[7] that by removing/excising the pseudocapsule embedded with GCT cells, along with extended curettage on bony surfaces, the recurrence rate could be brought down to almost negligible levels. Table four compares our study with others on GCTs managed with curettage and various adjuvants, showing the effectiveness of the pseudocapsule excision method in decreasing the rate of recurrence in giant cell tumors of the bone.

When reporting functional data in the oncology setting, the MSTS score is the most commonly used metric. Soares et al. conducted a systematic review of 11 reports on oncological outcomes of giant cell tumors (GCT).[24] They reported that the mean overall MSTS score was 88.9% (range, 75.6–95.0%), with a mean MSTS score of 90.1° (range, 85.7–94.3°) for the curettage group and a mean MSTS score of 85.6% (range, 75.6–95.0%) for the wide resection group. Table 4 also shows the mean MSTS score of various studies ranging from 87% to 94%. In our study, we observed a comparatively low mean MSTS score of 77%. This lower score can likely be attributed to the fact that all our patients had grade 3 GCT tumors, which were associated with preoperative extensive cortical destruction and substantial soft tissue expansion into nearby tissues. These factors likely contributed to the reduced MSTS score observed in our study.

In our study, we included cases of GCT with grade 3 Campanacci involvement and at least two intact cortical surfaces. Most of these cases had impending pathological fractures, with 8 having pathological fractures. Further curettage and high-speed burr weakened the cortices further. Consequently, we performed internal fixation in all our patients. Due to differences in the elastic modulus between bone cement and bone, stress post-surgery can cause gradual absorption of bone surrounding the cement, leading to cement loosening and instability. This can result in an unstable joint and intra-articular fractures. Internal fixation along with bone cement decreases the chances of this effect and the risk of post-operative intra-articular fractures.[7] However, bone cement, although strong in compression, is relatively weak when subjected to shear and torsional forces. Due to increased stress at trochanteric regions, bone cement may not withstand it. Therefore, we used bone grafting and internal fixation in 8 cases involving the proximal femur.[25]

Table 4. Comparison of oncological outcomes after extended curettage with various adjuvants in GCT

Author	No. of patients	Surgical technique	Campanacci classification	Mean MSTS Score	Local recurrence	Infection
Suzuki et al[20]	30	Curettage plus high-speed burr plus electrocauterization plus saline/water plus autogenous bone graft (18 patients) vs. curettage plus high-speed burr plus electrocauterization plus saline/water plus autogenous bone graft and PMMA(9 patients) vs. curettage plus high-speed burr plus electrocauterization plus saline/water plus PMMA (3 patients)	Grade I–10 pts; Grade II–10 pts; Grade III–10 pts	NF	33.3% (10 patients)	NF
Abdelrahman et al [21]	28	Curettage plus cryotherapy and bone graft (optional) plus PMMA (10 patients) vs. curettage plus cryotherapy plus bone graft (optional) plus PMMA and internal fixation with intramedullary hardware (18patients)	Grade I–10 pts; Grade II–14pts; Grade III– 4 pts	93.9%	3.6% (1 patient)	3.6%
Ayerza et al[6]	22	Curettage plus phenol plus cancellous bone plus structural allograft plus internal fixation (LCP plate)	Grade II–18 pts; Grade III– 4 pts	94.3%	9.1 % (3 patients)	0%
Saibaba et al[22]	36	Curettage plus phenol plus subchondral bone graft plus gel foam layer plus PMMA	Grade I – 2 pts; Grade II–18 pts; Grade III–16 pts	92%	2.8% (1 patient)	NF
Kundu et al[23]	26	Curettage plus high-speed burr plus electrocautery on spray plus autograft in the subarticular area plus gel foam layer and PMMA	Grade II–10 pts; Grade III–16pts	90%	11.5% (3 patients)	3.8%
Wu et al[11]	27	Curettage plus subchondral bone grafting plus PMMA	Grade I – 5 pts; Grade II –14 pts; Grade III– 8 pts	87.3%	3.7% (1 patient)	3.7%
Our Study	82	Extended curettage plus psuedocapsule excision with bone cement or bone graft	Grade III–82 pts	77%	0%	2.43 %

NF: data not found; PMMA, polymethyl methacrylate; LCP: locking compression plate

Post-operative infection was reported in only two cases, both affecting the proximal tibia at the medial condyle. These cases were managed by removing the infected implant and bone cement, followed by the reapplication of antibiotic-impregnated bone cement and a gastrocnemius myofascial flap. Infection was resolved in both cases at the final follow-up. The medial condyle of the tibia is situated practically in a subcutaneous location. After reconstruction, bone cement remains directly underneath the skin. Accumulated hematoma directly under the skin may cause skin necrosis or wound dehiscence, leading to cement exposure and infection. Since these were the initial cases, we started routinely covering the cement and implant with a gastrocnemius myofascial flap in all medial condyle tibia cases. No complications, such as wound dehiscence or infection, were noted in subsequent cases.
Our study had certain limitations. Primarily, the lack of a comparison group for assessing recurrence rates stands out as a significant shortcoming. Additionally, the study's focus on a single center and its inclusion of a relatively small number of patients are important limitations.

CONCLUSION

Extended curettage and pseudocapsule excision have the potential to decrease the recurrence rate of giant cell tumors of the bone. To ascertain the genuine impact of pseudocapsule excision on reducing recurrence rates and enhancing overall outcomes, further research involving a control group and a more diverse subset of patients is imperative.

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