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Clinical outcome of Giant cell tumor of bone in South Indian Population

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Abstract

Introduction: Inadequate knowledge still exists about Giant Cell Tumor of Bone (GCTB) incidence, treatment and prognosis and moreover, standard treatment has not been formulated till date. Hence, the objective of the present study is to assess the demographic characteristics, treatment modalities and its complications, post-operative functional outcome assessment and long-term prognosis of south Indian population with GCTB, treated from tertiary cancer center in Chennai.

Materials and Method: A retrospective study of prospectively maintained data was conducted in 33 GCTB patients treated at Government Royapettah Oncology Centre (Chennai) from January 2009 to December 2016. SPSS software of version 21.0 for windows was employed for statistical analysis.

Results: The mean age of the studied populations was 31.06 ± 10.83 years (range from 15 – 65 years, median-27 years). The mean duration of follow-up period was 9.6 ± 6 months (range from 2 to 24 months). The male to female ratio was 1:1.5(male: 13(39.4%) and Female (20 (60.6%). GCTB patients underwent treatment ranging from cryotherapy, intralesional curettage alone and wide local excision to resection with or without reconstruction with custom mega prosthesis for different anatomical locations.

Conclusion: From our analysis, we conclude that the GCTB patients of south India possess slightly different characteristics in terms of higher incidence in radial bone. In conclusion, resection with CMP reconstruction may be a suitable surgical option for advanced stage GCTB patients with reduced complication rate and provide good functional limb. Hence, devising an early identification and treatment strategy according to risk stratification becomes mandatory.

Keywords: Giant cell Tumor, Benign aggressive Bone tumor, CMP reconstruction

Introduction

Giant Cell Tumor of Bone (GCTB), originally described by Cooper and Travers in 1818,[(1)] is a primary intra-medullary benign bone tumor that possesses mononuclear stromal cells and characteristic multinucleated giant cells. It commonly occurs in the epiphyseo-metaphyseal region of long bone (lower extremities around the knee) and has erratic aggressive nature with high recurrence rate.[(2,3)] It has a tendency for metastases to the lungs (1-9%) or lymph node (uncommon) or to undergo malignant transformation.[(4)] The initial treatment involves complete eradication or excision of the tumor with an aim to preserve joints.[(5)] This lead to the development of various surgical methods such as curettage with high-speed blur, adjuvant therapy using phenol and en bloc resection but the drawbacks were recurrence (60%) and large bony defect reconstruction.[(6)] The use of Custom Mega Prostheses (CMP) has overcome the above limitations. The objective of the present study is to assess the demographic characteristics, treatment modalities and their complications, functional assessment and long-term prognosis in GCTB patients of south Indian region.

Materials and Method

This is a retrospective study of the prospectively maintained database of GCTB patients from January 2009 to December 2016. All the clinical data of patients were retrieved from Medical Records Department (MRD) of our institution. The patients were followed up at regular intervals. The designed proforma contained the details of clinical examinations, radiological evaluation, surgical management and histopathology. X-ray and MRI scan information were available in all patients' records. Lesion location, size of the radiolucent area, Campanacci grading and Enneking's system were also recorded. Musculoskeletal Tumor Society scoring system (MSTS) functional outcome scoring system was employed to evaluate the functional assessment in post-operative-patient after limb-preserving surgery. Patient's functional assessment were recorded after a minimum of 6 months from the postoperative period. Statistical Package for the Social Sciences (SPSS) software was employed for statistical analysis.

Results

Among 114 patients who visited our department with bone tumors during the study period from January 2009 to December 2016, only 33 patients were diagnosed as GCTB and their records were analyzed retrospectively. All the patients were followed up regularly in our institution. The incidence was about 28.9%, which included both primary and recurrent GCTB. The average follow-up period was 9.6 + 6 months (range from 2 to 24 months). The mean age of the studied population was 31.06 ± 10.83 years (range

from 15 – 65 yrs, median 27 yrs) and their age wise distributions are enlisted in Fig. 1. The male to female ratio was 1**:**1.5 [male: 13(39.4%) and female: 20 (60.6%)].

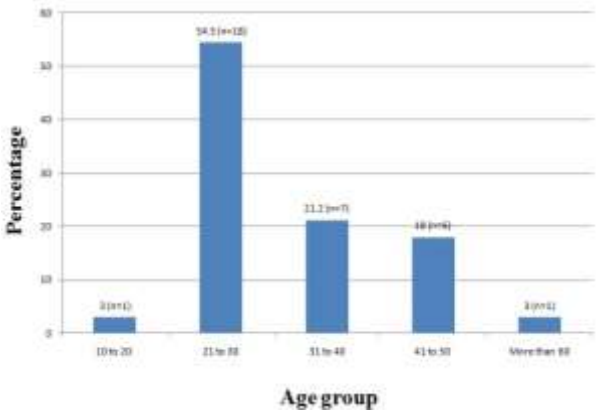

Fig. 1: Age Wise Distribution of the Study Population

The predominant site of the lesion was observed in proximal end of the tibia (30.3%), distal end of radius (21.2%), femur (18.2%) and rest of the lesions are depicted in the Fig. 2.

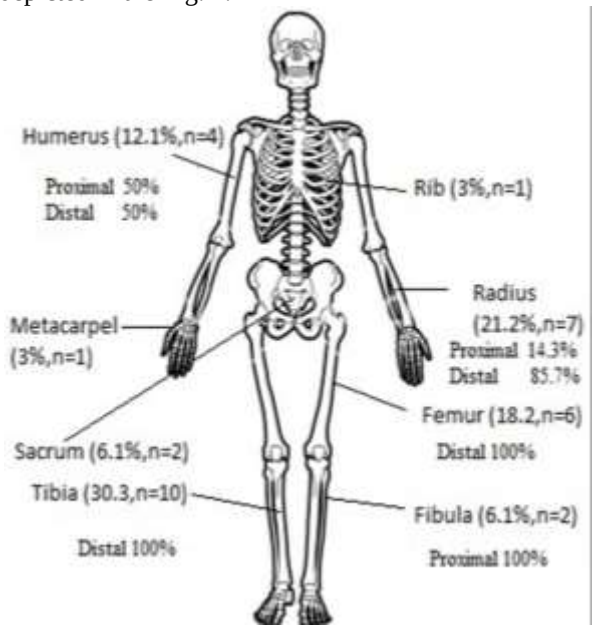

Fig. 2: GCTB of bone Anatomical Distribution

Table 1 shows the clinical and radiological data of the retrospectively analyzed patients. All 33 patients in our study had epiphyseo-metaphyseal site disease. There was no statistical significance between the two grading systems.

Table 1: Clinical and Radiological presentation

Assessment	Stage at presentation	No. of patients (%)
Enneking staging	Stage -I	5 (15%)
	Stage -II	8(24%)
	Stage- III	20 (60%)
Campannacci grading	Grade -I	5((15%)
	Grade -II	10(30%)
	Grade- III	18(55%)

The lesion sizes were estimated as size less or more than half the width on A-P radiograph and were compared between the primary lesion and recurrent disease presentation group. From our analysis, we observed no significant (p=0.503) difference between the two groups (primary and recurrent group) as may be the late presentation of primary group to our centre. In a total of 33 patients, 12 (36.4%) patient had lesion size less than half of the width and majority of 21 patient (63.6%) had more than half the width of the bone circumference as described in Table 2.

Table 2: Size of the lesion

Disease	Size of the lesion	No. of patients (%)
Primary GCTB	Less than half of width	9 (27%)
	More than half of width	16(48%)
Recurrent GCTB	Less than half of width	3(9%)
	More than half of width	5(15%)

The mean size of the tumor was found to be 8.91 cm X 8.38 c.

In our series, we have observed that 8 patients (24%) had pathological fractures at the time of presentation. In a total of 33 patients, 16 (63.4%) patients underwent resection with CMP reconstruction, 3 patients (7.3%) underwent resection with fibular sturt reconstruction, 4 (7.3%) patients had wide local excision, 1 patient underwent intralesional curettage and 2 patients had sacrectomy as shown in Table 3.

Table 3: Procedure done- Anatomical site wise

S. No	Site of bone GCTB	Procedures done	Nos.	Total
1	Tibia	1. Intralesional curettage and bone grafting	1	10
		2. Proximal tibial resection with CMP	6	
		3.Above knee amputation with skew flap	1	
		4.Chemotherapy (weekly peg interferon)	1	
		5. Cryosurgery	1	
2	Radius	1.excision of fibular graft with external fixation 2.excision of proximal radius bone 3.Distal radial resection with centralization of ulna	1 1 1	7
		4. Distal radial resection and fibular sturt reconstruction /graft	3	
		5. wide local excision and groin flap	1	
3	Femur	Distal femoral resection +CMP reconstruction	6	6
4	Humerus	1. proximal humeral resection with CMP	2	4
		2. distal humeral resection & CMP	2	
5	Fibula	Wide Local Excision	2	2
6.	sacrum	Sacrectomy -staged procedure	2	2
7.	Metacarpal	Excision of metacarpal bone /bone graft and external fixator	1	1
8.	Rib	Chest wall resection	1	1

Out of 33 patients, 12 (36.4%) had developed post-surgical complications. The distribution of complications among 12 patients who had complication is represented Fig. 3.

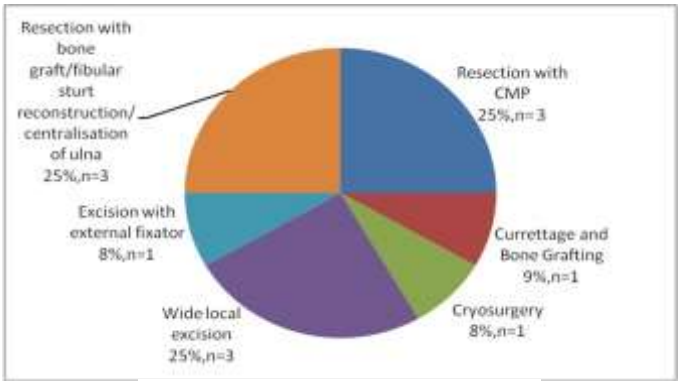

Fig. 3: Post-Surgical Complications

Out of 16 patients who had undergone resection with CMP, 18.8% (n=3) population developed post-operative complications out of which 1 patient (6.25%) had soft tissue, 1 patent had joint contracture and 1 patient had CMP fracture at tibial shaft and stem junction. Among the patients who had undergone external fixation (n=2), 50% of the population had exfix slipped as a complication (n=1). Among the wide local excision patients, 50% of the population had a complication of recurrence. Rests of the complications are negligible. Table 4 provides the information of complications related to the type of surgery involved.

Table 4: Surgical Complications

S. No	Type of surgery (numbers)	Complications	No. of patients (%)	Total Percentage (%)
1	Resection with CMP (16)	Soft tissue infection Joint contracture Periprosthetic fracture	1 (6.25%) 1 (6.25%) 1 (6.25%)	18.8
2.	Curettage and bone grafting (1)	Recurrence	1 (100%)	100
3.	Cryosurgery (1)	Sinus formation	1 (100%)	100
4.	Wide local excision (4)	Recurrence Foot drop	2 (50%) 1 (25%)	75
5.	Excision with external fixator (2)	Ex fix slip	1 (50%)	50
6.	Resection with bone graft/ fibular sturt reconstruction /centralisation of ulna (5)	Recurrence Deformity Foot drop	1 (20%) 1 (20%) 1 (20%)	60

Among 33 patients, 24.2% (n=8) of the population had the recurrent disease at presentation and rest of the population had primary lesion (75.8%, n=25). The Mean age of the patients with the primary disease was 31.36 + 11.38 years (range from 21-65 years). There was no difference in male: female ratio (1:1.08). Majority of the patient's presented with Campanacci grade -III features (n=15, 60%), campanacci grade II (n=8, 32%) and grade-I (n=2, 8%). The incidence is found to be 21.9%.

The incidence of the recurrent population in our centre was found to be 7% and their mean age was found to be 30.13 +9.6 years (range from 15-42 years). The male (12.5%): female (87.5%) ratio was 1:7. All recurrent GCTB patients presented with campanacci grade III features. Table 5 presents the lesions involvement site between primary and recurrent patients. In both the groups, lesions with tibial and radial involvement are predominant.

Table 5: Primary Vs Recurrence disease presentation

Nature of disease	Site wise distribution	No. of patients	Percentage (%)
Primary	Tibia	8	24.4
	Radius	4	14.6
	Femur	4	14.6
	Humerus	3	7.3
Recurrent	Tibia	2	6.06
	Radius	3	9.01
	Femur	2	6.03
	Humerus	1	3.02

Table 6: Primary surgery done for recurrent GCTB

S. No	Site of GCTB	No. of patients (%)	Previous surgeries	Disease free survival
1	Proximal Tibia	2 (25%)	1. Currretage and bone grafting 2. Curretage and Bone grafting	2 years 4 months
2	Radius	3 (37.5%)	1. Wide local excision with fibular graft 2. Curettage twice 3. Wide excision	7 months 2 years 2 years 2 months
3	Femur	2 (25%)	1. Femur lateral condyle curettage and cementing 2. Femoral resection	12 years 5 years
4	Humerus	1 (12.5%)	Curettage and bone grafting	1 year

The histories of previous surgery underwent by the recurrent group are enlisted in Table 6 and their mean duration of the disease free interval was found to be 37.6 months (range from 4 to 144 months) Fig. 4 represents the distribution of previous surgeries underwent by the recurrent population group.

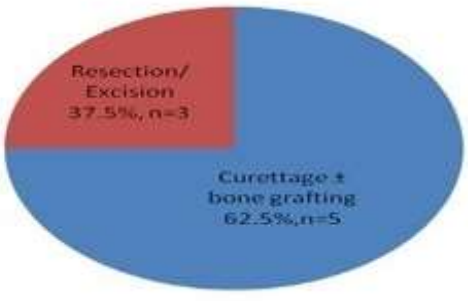

Fig. 4: Information of previous surgery underwent by recurrent group

In short, curettage alone and resection/excision treatment had recurrence of 62.5% (n=5) and 37.5% (n=3) respectively.

MSTS was used to assess the functions of operated limb in post-operative patients, those who underwent endoprosthetic reconstruction procedure.[9] We have found that 80.5% of the patients had the good score of 27 points and 19.5% of the patients had an intermediate score between 15 to 18 points.

All the patients were discharged in stable conditions. They were on regular follow-up for an average period of 9.6 ± 6 months (range from 2 to 24 months).

Discussion

GCT contributes to 3-4% of primary bone tumors especially in the distal femur and proximal tibia followed by the distal radius.[5] The epidemiological studies show that GCT accounts for 5% of all primary tumors and 21% of benign tumors in the US and Europe.[10] A recent study from large population

database established that Chinese populations are more prone for GCT than Americans.[11] The incidence of GCT was reported to be higher in oriental and Asian than other population and represent around 20% of skeletal neoplasms.[12] Usually, GCTB patients present with mobility impairment and pain caused due to bone destruction and they are at the risk of fracture.[13] Enneking staging and radiographic grading system (Campanacci's Grading) were well elucidated to confirm the pathological or severity of the lesions and are the ideal tools for planning of surgical treatment.[7,8] Mesenchymal stromal cells transformation leads to the origin of GCT and is responsible for unpredictable behavior. A limited number of researches especially in Asian population have further enhanced the problem of devising a standard protocol for the GCTB treatment. Previous reports around the world suggest that GCT contributes to the primary bone tumor in US, north India and south Indian population as 5-7%, 9% and 30% respectively.[14,15] The Incidence of GCTB is much higher in Indian population as against western population. Our study has shown that incidence of GCTB is around 28.9% which coincides with previous studies.

Earlier investigations had shown the mean age to be 26.8 yrs (16-50).[16] Even though current literature supports for the higher occurrence of GCTB with 20-39 years, a significant subset of our study population lies beyond this (1 patient below 20 years and 6 patients above 40 years).[17] In our study, we have observed that the mean age of the patients with primary disease was 31.36 + 11.38 years (range from 21-65 years, median 26 years and mean age among patients with recurrent disease was 30.13 + 9.6 years(range from 15-42 years) which is similar in data obtained by Saikia KC *et al* in 2011.[18] The commonest presentation of GCTB was reported at third decade of life (16) from earlier papers in similar to our study of patients.

Our study had shown that GCT affects mainly female population compared to male population as similar to the Dahlin D.C. Caldwell's previous paper and contrary to a large number of studies including Indian literature data.[16,19-21]

It has been well established that GCT primarily affects the ends of long bones and our study agrees with the finding that 87.8% (n=29) of our study population had lesions in long bones.[22] Anatomical analyses of the bone lesion in our study have shown that all patients had lesions present only in the proximal areas of both tibia and fibula bone, but on analyses of the long bone lesion in our study, out of 29 patients (100%), 10 patients (34%) with disease in proximal tibia, 6 patients (20%) in distal femur (proximal femur-0%) and 7 patients (24%) in distal radius, 4 patients(13%) in humerus (6.5% in proximal and 6.5% in distal humerus respectively) and 2 patients(6%) in fibula. But reported literature suggests that usually distal femur and proximal tibia are involved in 50 to 60% of the population and about 10% of the populations are affected at the distal radius (22-24). Our reports are concurrent with the previous findings except in case of the incidence of radius bone and humerus bone involvement. The previous report had shown that proximal femur and humerus are involved in less than 10% of the cases[25-29] which is contrary to our study where all of our femur bone patients had lesion distally. Moreover, our humerus patients had an equal distribution of 50% involvement in both proximal and distal region.

Our series of patients had a higher incidence of pathological fracture at presentation (24%) than the reported data in the range of 2 to 22.4%.[7,13,30-31] Local recurrence is the major issue encountered in the management of GCTB patients after surgical treatment. Literatures had projected the recurrence rate varies from 27% to 65% after isolated curettage, 12-27% after curettage with adjuvants (high speed burr, phenol, liquid nitrogen or Polymethylmethacrylate (PMMA)) and 0-12% after en bloc resection.[7,32-34] In our study, all of our patients who had undergone isolated Intralesional curettage had the recurrence (n=1) while 50% of the population developed the recurrence after wide excision (50% recurrence, n=2) and 20% had recurrence after resection (20%, n=1). We had not observed any recurrence in post-operative CMP patient.

Li D *et al* studied a total population of 179 patients to assess the parameter that could influence the local recurrence in GCTB patients and observed that the disease-free interval to be 60 months (5 years) in patients who had wide resection surgery alone.[35] Another study by Van der Heijden L determined the recurrence-free survival rates at 2 and 5 years and was found to be 0.82 and 0.74 respectively.[36] Our study analysis of recurrent group population correlates with the previous findings and we had observed the mean disease-free interval time to be 37 months (3 years).

Authors have identified the potential risk factor for local recurrence as Cortex destruction, soft tissue extension, pathological fractures, young age and location in the distal radius.[31,32] Our finding coincide with the report as majority of our recurrent group patients falls in the age group between 20 to 30 years (50%, n=4) also had significant pathological fractures (50%) with higher involvement in the distal radius. In contrast, Van der Heijden L *et al* concluded that age, sex, location and pathological fractures are not the risk factor for local recurrence except soft tissue extension.[36]

Thakur S *et al* and many other authors had demonstrated the usefulness of CMP procedures for campanacci grade-2 and 3 tumors with soft tissue involvement and pathological fracture compared over curettage and wide excision.[5,37] Moreover, authors have stressed that best initial treatment option would be a resection with CMP reconstruction as this prevents repeated surgeries / amputation. Our study has also

shown the benefits of CMP procedure employed in our populations. Hence, En bloc resection and reconstruction with CMP seems to be a viable option among limb-sparing surgeries with least recurrence rates and good functional outcomes in recurrent GCTB.

Conclusion

From our analysis, we conclude that the GCTB patients of south India possess slightly different characteristics in terms of higher incidence in radial bone. This study has documented the incidence of primary GCTB in 65 year old patient, female gender propensity, major involvement of long bones and no recurrence with CMP reconstruction. Young age, pathological fracture and distal radius site may be risk factors for local recurrence. The rising incidences of GCTB in our population necessitate us to select appropriate treatment as it decides patient outcome. Disease stage and the selection of surgical treatment for suitable patient determine the long term oncological results. In conclusion, resection with CMP reconstruction may be a suitable surgical option for advanced stage GCTB patients with good post operative rehabilitation to have good functional limbs. Further studies need to be conducted on larger number of population (multi-centric studies) in-order to formulate better treatment protocol for locally recurrent tumors. This tumor occurs during the productive period of life which in turn can affect the quality of life. Hence, devising an early identification and treatment strategy according to risk stratification becomes mandatory.

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