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ORIGINAL ARTICLE

Retrospective Audit of Various Surgical Modalities Adopted for Giant Cell Tumor in a Rural Tertiary Cancer Center

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Abstract

Giant cell tumor of bone (GCTB) is a rare tumor with a spectrum of clinical behavior. Standard treatment modalities include surgical curettage to wide resection, and varying oncological and functional results have been reported. The aim of this study was to evaluate the functional outcome and recurrence rates of patients who underwent surgery for giant cell tumor in a rural tertiary cancer center from June 2009 to December 2016. A retrospective review of 12 patients (7 males and 5 females) with GCT of the extremity bones treated in the institution between the period of June 2009 and December 2016 was performed to study the oncological and functional outcomes. All patients were evaluated by clinical examination, plain X-ray of local parts, X-ray of the chest, and MRI of local parts. A biopsy was taken in all cases to confirm the diagnosis. All patients underwent surgical treatment including curettage combined with cryosurgery and bone cement or wide resection and reconstruction. Selection of the surgical technique was based on the site and size of the lesion, soft tissue involvement (intra- or extra-compartmental), and if recurrent or not. The patients were followed up to April 2018. The mean age of the patients was 31.3 years. The tumor sites were distal femur in 3 cases, proximal tibia in 6, ischial bone in 1, distal radius in 1, and 1 in the metacarpal bone. Campanacci radiographic grading was grade1 in 3 cases, grade 2 in 2 cases, and grade 3 in 7 cases. Out of 12 patients, local recurrence was noted in 2 patients (16.7%). Functional evaluation was performed according to the Musculoskeletal Tumor Society Scoring (MSTS) system. Mean MSTS score was 25. To preserve the good function of the extremities and avoid local recurrence, we consider that curettage with adjunctive therapy such as polymethylmethacrylate (PMMA) and liquid nitrogen should be employed for the treatment of benign GCT of bone. Wide excision should be considered for large tumors where achieving oncological results with functional preservation would be difficult with curettage procedure.

Keywords Giant cell tumor of bone · Musculoskeletal Tumor Society Scoring (MSTS) system · Extended curettage

Introduction

Giant cell tumor of bone (GCTB) is a relatively rare, benign but locally aggressive osteolytic skeletal neoplasm of young adults. First recognized in 1818 [1], it was not until 1940 that GCTB was formally distinguished from other tumors of the bone such as aneurysmal bone cyst, chondroblastoma, and nonossifying fibroma [2]. Nearly half of the lesions are reported to involve the region around the knee (50–55%), while 10% are associated with the distal end of the radius [2, 3]. Pathological fracture occurs in 6–10% cases, and primary malignant GCT has been reported in 1% cases [2, 4, 8]. About 10% of cases result in distant metastases, usually to the lungs [5, 8]. Enneking's surgical staging system [3] and Campanacci and co-workers' radiographic grading system [4–6, 14] have provided better methods of evaluating and

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comparing the results of the treatment. The standard treatment has ranged from surgical curettage to wide resection, and varying results have been reported for all modalities [7–11]. The purpose of this study was to evaluate the functional outcome and recurrence-free survival (RFS) of patients who underwent surgery for giant cell tumor in Malabar Cancer Centre from June 2009 to December 2016. The institution is located in a rural area with little orthopedic backup. All the surgical managements were performed by a senior surgical oncologist who is trained in orthopedic oncology.

Materials and Methods

There were 12 patients with giant cell tumor of bone, treated between 2009 and 2016. All patients were worked up with X-ray and MRI of the local part and CT thorax in selected cases. All the slides of biopsied, excised tumors were reviewed, and the diagnoses were confirmed by a pathologist. Local recurrence was evaluated by the most recent radiogram or by interviewing the patients on the telephone. The treatment was decided based on the clinico-radiological features. The operative techniques included adequate exposure, meticulous curettage with burr drilling, and cryotherapy with 2 to 3 cycles of freezing and thawing and reconstruction with polymethylmethacrylate (PMMA) application to fill the defect which is described under.

Exposure

After exposure of the involved bone and soft tissues, a cortical window was created in the tumor site. Generally, the size of the window is decided to enable complete curettage of the cavity. To minimize additional bone loss, the tumor is approached through the retained thinned or destroyed cortex. A large cortical window is essential to expose the entire tumor and avoid inadequate curettage. The window is made elliptical to provide adequate exposure of the cavity. The axis of the ellipse is made along the long axis of the bone to reduce the stress effect.

Curettage

The curettage included initial curettage with curette till all gross disease is removed followed by smoothening of crevices within the cavity with burr drill. The irregularity makes it virtually impossible to remove all the tissue from the inner reactive shell with a curette. Hence, high-speed burr drilling is used. Care should be taken to avoid injury underneath major neurovascular structures.

Cryosurgery

Before the introduction of the liquid nitrogen, the surrounding skin, soft tissues, and neurovascular bundle are protected. Using the open system, liquid nitrogen is poured through a stainless-steel funnel into the tumor cavity. Care is taken to fill the entire cavity. Liquid nitrogen is left in the cavity until it has completely evaporated with care being taken to avoid spillage. Two to three freeze-thaw cycles of liquid nitrogen are used at the end of each of which the cavity is irrigated with normal saline or betadine solution.

Reconstruction

Reconstruction is performed using PMMA. Soft tissue flaps were used in the periarticular areas. Skin flaps were closed after placing a suction drain. Reconstruction was individualized according to the age of the patient, the location of the tumor, the functional demands, and the preference of the patient [12, 13]. Wide resection was done in large tumors where achieving oncological results with functional preservation was difficult with curettage procedure. This en bloc resection included the entire lesion with the reactive zone and a cuff of normal tissue to ensure a good safety margin. In such cases, metal prosthesis was used for reconstruction.

Functional Evaluation

Functional evaluation of 12 patients was performed according to the scoring system of the Musculoskeletal Tumor Society (MSTS) [15]. Functional analysis was performed at the most recent follow-up visit.

Statistical Analysis

Data expressed in number, percentage, mean, and standard deviation. For calculating the recurrence-free survival, Kaplan-Meier estimate is used. The correlation was found by using the Spearman method. For all statistical analyses, a P value of < 0.05 was considered significant.

Results

Out of 12 patients, 7 (58.3%) were males and 5 (41.7%) were females. Five (41.7%) presented with pain, 5 (41.7%) presented with swelling, and 2 (16.7%) presented with pathological fracture. Seven cases (58.3%) were primary and 5 (41.7%) were recurrent. All patients were biopsy-proven GCT, and all were of single site. Extended curettage was carried out in 8 patients (66.6%), and wide resection was performed in 4 patients (33.3%). Seven patients (58.3%) underwent reconstruction with PMMA and cryotherapy with liquid nitrogen

(Marcove's procedure) as an adjunctive procedure, 3 patients (25%) with bone prosthesis, 1 (8.3%) with PPMA alone, and 1 (8.3%) with soft tissue flap. Distribution of cases is shown in Table 1. Mean tumor size was 6.7 cm. Soft tissue involvement was seen in 6 (50%) patients. Ten (3.3%) patients had R0 resection and 2 (16.7%) patients had R1 resection. Mean MSTS score was 25. Mean and median of different variables are shown in Table 2.

Local recurrence was seen in two (16.7%) patients. Median interquartile range (IQR) of RFS was 25 months (19.7, 46.7). Estimated 5 years RFS was 81.5% with Fig. 1 showing RFS Kaplan-Meier curve. Correlation between RFS and different variables are as shown in Table 3. Two out of the eight patients who underwent extended curettage suffered a local recurrence. There was no local recurrence in the group of patients receiving wide resection as their initial surgery. Out of six patients with soft tissue involvement, two patients recurred and none without soft tissue involvement. One patient recurred within 4 months. He was given nine doses of monthly denosumab and then taken up for limb salvage surgery with bone prosthesis. Another case recurred after 2 years. No correlation found between MSTS score and type of surgery or adjunctive used. None of the patients received any adjuvant therapy. None of them had distant metastasis on follow-up, and all were alive.

Discussion

The high rate of local recurrence following initial surgery has led the investigators to use different surgical modalities for the treatment of GCT according to the stage of the disease aiming at decreasing the rate of local recurrence along with good functional and cosmetic results [16]. Simple curettage involves intralesional curettage alone. Extended curettage is a technique of intralesional curettage where the margins of the excision are extended by a surgical, chemical, or thermal adjuvants. The use of physical adjuvants as cryosurgery and phenol in combination with curettage together with the use of bone grafts and bone cement preserves the shape and strength of the bone which helps to achieve good results and limits the indications of resection and amputation. Bone cement compared to bone grafts provides immediate support and allows for intensive curettage even of large tumors [17].

Cryosurgery extends the margin of simple curettage and makes it biologically equivalent to wide intra-compartmental resection. Cryosurgery entails using a wide excision in situ but without the morbidity of en bloc resection and spares adjacent joint with a low rate of local recurrence [18]. Corticocancellous grafts are required to strengthen the subcortical bone, whereas fibular struts are used for cortical defects [19].

With respect to curettage and bone cement, the reported rate of local recurrence by O'Donnell et al. using curettage and bone cement was 33.3% that decreased to 16.6% when mechanical burr was used, so they recommend using the burr at the end of the procedures [20]. Curettage and cryosurgery with bone cement were done in eight patients in our study, with local recurrence occurring in two cases (25%). This result was not in harmony with the results of other authors who reported recurrence rates lower than 15% in cases of GCT treated with curettage and cryosurgery [18, 19]. Four patients underwent wide excision in our study, and none of them recurred, which was in harmony with the result of other authors [21]. No correlation found was found between RFS and other variables such as age, sex, location, fracture, treatment modality, soft tissue involvement, R0 resection, and adjuvant used. This may be due to the small

Table 1 Distribution of cases

Case	Age (years)/gender	Site of the tumor	Type of surgery	Adjunctive used	MSTS score	DFS (months)
1	29/M	Distal femur	Limb salvage surgery	Prosthesis	15	37
2	29/M	Proximal tibia	Extended curettage	PMMA + liquid nitrogen	30	24
3	25/F	Proximal tibia	Limb salvage surgery	Prosthesis	28	24
4	36/F	Metacarpal bone	Wide local excision	Soft tissue flap	27	33
5	37/F	Distal radius	Extended curettage	PMMA + liquid nitrogen	30	19
6	36/M	Proximal tibia	Extended curettage	PMMA + liquid nitrogen	13	22
7	33/F	Ischial tuberosity	Extended curettage	PMMA alone	30	75
8	25/F	Proximal tibia	Limb salvage surgery	Prosthesis	27	72
9	32/M	Distal femur	Extended curettage	PMMA + liquid nitrogen	27	50
10	32/M	Proximal tibia	Extended curettage	PMMA + liquid nitrogen	30	15
11	18/M	Proximal tibia	Extended curettage	PMMA + liquid nitrogen	22	04
12	44/F	Distal femur	Extended curettage	PMMA + liquid nitrogen	22	27

Table 2 Mean and median of different variables

Variable	Mean (SD)	Median (IQR)
Age (years)	31.3 (± 6.8)	
MSTS score	25.08 (± 5.9)	
Size (cm)	6.7 (± 3.5)	
Recurrence-free survival (months)		25 (19.7, 46.7)

SD standard deviation, *IQR* interquartile range

Table 3 Correlation between RFS and other variables

Variable	*P* value
Type of surgery	0.317
Soft tissue involvement	0.403
Size of tumor	0.858
R0 resection	0.304
Adjunctive used	0.063
MSTS score	0.530

sample size, and one case which recurred after 2 years should have undergone wide resection but because of the physical condition of patient (cerebral palsy), extensive procedure was avoided.

Bone resection is not usually recommended because of its associated significant morbidity. It is indicated in the proximal radius and fibula and distal ulna, tubular bones of the hand and foot, coccyx, sacrum, and pelvic bones, also in situations in which 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. Amputation was reserved for massive recurrence or in malignant transformation where limb salvage surgery was not feasible.

Radiation therapy is not used as adjuvant treatment because of concerns regarding the efficacy of therapy and risk of sarcomatous change after radiotherapy [22]. Radiotherapy can be used as an alternative to surgical option in cases that cannot be treated with surgery or left with severe disfigurement after surgery. In our study, we did not use radiotherapy in the treatment of our patients [23]. The rate of pulmonary metastases in our study patients was 0%, similar to previous reports reporting ranges from 0 to 4% [24]. Our functional results were comparable with those reported in the literature for all adjuvants. Mean MSTS score was of 25 (range, 13 to 30) after the use of liquid nitrogen and PMMA [25, 26].

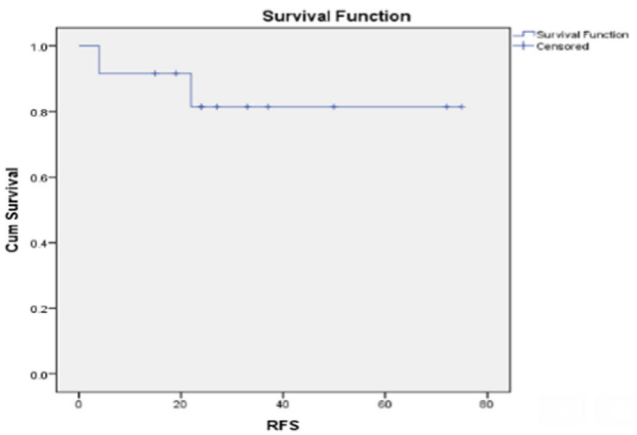

Fig. 1 RFS Kaplan-Meier curve

Conclusion

Primary treatment of GCT is surgery, the type of which depends on preoperative evaluation which includes clinical evaluation that involves the size and site of the tumor in relation to surrounding structures. Routine evaluation consists of plain X-ray and MRI of the local part with optional CT (thorax) scan. Curettage alone may result in a high rate of local recurrence. On the other hand, curettage and adjuvant cryosurgery with bone cement or bone grafts give a lower rate of local recurrence. Resection is recommended for cases where resection results in no significant morbidity as proximal fibula and flat bone or in extremely large lesions where achieving oncological results with functional preservation will be difficult with curettage procedure.

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