The role of cryosurgery and cement packing in treatment of giant cell tumor of bone in lower limb.

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Abstract

Background
Giant cell tumor (GCT) of bone is one of the commonest benign bone tumors with a high incidence of local recurrence after surgical treatment. This study aimed at evaluating the technique of extended curettage as a surgical treatment of GCT of the bone of the lower limb as regard the functional and oncological outcome.
Patients & Methods
Twenty patients with primary GCT of bone of lower limb had been treated by extended curettage using the high-speed burr and LN (as an adjuvant). Reconstruction was performed using bone cement ± graft± internal fixation. The follow up period ranged from 24 to 42 months (mean of 28.6 months±2.12) to assess the functional outcome (using musculoskeletal tumor society functional scoring system) and to detect the presence of complications especially the local recurrence.
Results
The mean age was 31.55 years. The distal femur was affected in 45% of cases; proximal tibia (40%) and distal tibia (15%). 4 patients were Campanacci grade I, 10 patients were grade II and 6 patients were grade III. The mean functional outcome at final follow up was 28.05±1.09. Local recurrence occurred in two cases (10%).
Conclusion
The use of extended curettage as a treatment of GCT of bone resulted in good functional outcome, decrease the local recurrence rate, and limit the indications of wide resection.

Key words
GCT of bone, extended curettage, high speed burr, cryotherapy, direct pour method, liquid nitrogen, bone cement
Level of Evidence: Level IV, case series.

Introduction

Giant cell tumor (GCT) of bone is one of the commonest benign bone tumors with a high incidence of local recurrence after surgical treatment. [1-4], It commonly affects the ends of long bones, about 40% of lesions occur around the knee joint but almost all joints could be involved. [4-7]

Although the way of treatment of giant cell tumor is still of controverse, it has an unpredictable behavior regarding the local recurrence and pulmonary metastasis not always related to radiographic or histological appearance, the aim of surgical treatment in such cases is to eradicate the tumor, preservation of normal articular and bony architecture, decrease the need for wide resection. [5,8]

Many surgical procedure were tried to solve this problem like simple curettage which often results in a high local recurrence rate (27-55%), whether bone graft was used or not, while in wide resection there is low recurrence rate but there is a significant impairment of patient's joint function. [4,9]

It was proved that the use of power burrs and local adjuvants as phenol, liquid nitrogen, bone cement, hydrogen peroxide, zinc chloride, and argon beam cauterization carries a significant rate of cure and decrease the rate of local recurrence. [5]

Marcove et, al. had developed the usage of cryotherapy in the treatment of giant cell tumor of the bone and described the effectiveness of a direct pour method in freezing the walls of a curetted cavity. [10]

The aim of this study was to evaluate the technique of extended curettage as a surgical treatment of GCT of the bone of the lower limb as regard the functional and oncological outcome.

Patients and Methods

Twenty patients with primary giant cell tumor of bone of lower limb were included; they had been treated by

the technique of extended curettage of the bony lesion.

The current study was conducted between January 2013 to August 2015 after approval of the Research Ethics Committee of the university.

All patients with primary GCT of bone of the lower limb of any grade (Campanacci's grades I,II or III) with a cortical break confined only to one surface and less than one third of the bone circumference on CT scan assessment were included in the study. [11]

Any cases with local recurrence or cases with pathological fractures, marked soft tissue extension or intraarticular extension were excluded from our study.

There were 8 males (40%) and 12 females (60%). A higher frequency of distal femur affection was present; representing 9 patients (45%) followed by proximal tibia 8 patients 40% and distal tibia 3 patients 15% respectively.

Regarding Campanacci's(11) radiological grading; 4 patients were grade I (20%), 10 patients were grade II (50%) and 6 patients were grade III (30%).

Reconstruction was carried out in all patients as follow: bone cement only in 7 cases (35%) while bone cement and impaction iliac bone graft were done in 13 cases (65%). Reconstruction was augmented by intramedullary hardware in 16 cases (80%) (Campanacci's grades II and III).

Complete clinical examination and investigations (Plain X ray, CT scan on the tumour, MRI and CT scan on the chest) were done for each patient, for diagnosis and staging of the bone tumor. Closed percutaneous tissue core biopsy (CT guided) was done in all cases to confirm the diagnosis, laboratory investigations were performed for such patients as a routine to prepare the patients for the surgical operation.

Staging of the tumour was done using Campanacci's radiological grading method as follows: intraosseous lesions with normal cortex were classified as grade I while grade II tumors were intraosseous lesions with a thin cortex but without loss of cortical continuity. Grade III tumors were extraosseous lesions that broke through the cortex and extended into soft tissue.[11]

Operative technique:

Extended curettage using the high speed burr with the use of liquid nitrogen (as an adjuvant therapy) and reconstruction (using bone cement ± bone graft) was done together with internal fixation with intramedullary rods whenever indicated.

Under general or spinal anesthesia, the patient lie supine on the table, A pneumatic tourniquet was used in all cases to decrease bleeding and to prevent blood from acting as a thermal barrier (as cryosurgery was performed in all cases). The affected lower limb was draped; under the guide of image intensifier, a cortical bone window was made through the weakest wall after exposure and examination of the bony cortices, the window must be large enough to expose the entire tumor (Fig.1A).

All gross tumor tissues were removed by hand curette. (Fig.1B, C). A high-speed burr was then used to ensure complete tumor removal (Fig.1D). the high speed burr has both thermal and mechanical effect on the tumor wall. great care was taken to preserve the subchondral bone as possible.

Before introduction of liquid nitrogen (LN), any bony perforations were identified and sealed, and the surrounding skin, soft tissues and neurovascular bundles were protected using gel foam and gauze soaked with warm saline (Fig.1E). we had follow the steps of direct pour technique described by Marcove (10) in every case (Fig.1F, G).

Through a stainless steel funnel, LN was poured into the tumor cavity with continuous irrigation of the surrounding soft tissues with warm saline to avoid thermal injury. The freezing and thaw cycles were repeated twice; with each cycle lasted for about one to two minutes and spontaneous thaw was allowed to occur for 3 to 5 minutes. The cavity was then irrigated with normal saline and hydrogen peroxide.

After the entire tumor had been removed, reconstruction of the remaining bone defect was performed. Polymethyl methacrylate bone cement was used as space filler (Fig.1 H). In addition of being filler, the bone cement has thermal and toxic effects.

In case of affection of weight bearing articular surfaces by curettage, a thin layer of autogenous corticocancellous iliac bone graft was placed over the exposed subchondral bone and the remainder of the cavity was filled with bone cement.

While in cases of Campanacci's grades II or III, reconstruction was augmented by intramedullary hardware. The tumor mass was sent for histopathological examination to confirm the diagnosis (Fig.2,3) then the tourniquet was removed, and good haemostasis was then ensured. The wound was closed in layers with suction drain.

Fig 1(A-I): Intraoperative steps; **A:** Cortical window was done in distal tibia to expose the tumour. **B and C:** The use of hand curette. **D:** The use of high-speed burr. **E:** The use of gel foam to protect skin and soft tissues before introduction of liquid nitrogen. **F and G:** the use of liquid nitrogen by the direct pour technique**. H:** After application of bone cement. **I:** The gross specimen after curettage.

Fig.2 (A-E): A: Anteroposterior and lateral radiograph of proximal tibia showing osteolytic lesion affecting the medial tibial condyle, reaching to the subchondral bone. **B**: CT showed the lesion without cortical breaching. **C:** MRI showed that the tumour is intraosseous with no soft tissue extension. **D:** The immediate post operative x-ray. **E:** 26 months follow up x-ray showing no signs of local recurrence.

Fig. 3 (A-B): A: plain x-ray A.P and lateral of distal tibia showed osteolytic lesion that reached to the subchondral bone. **B:** follow up x-ray with no evidence of local recurrence.

Postoperative management

The patients administrated injectable antibiotics like cephalosporins, analgesics as injectable non-steroidal anti-inflamatory drugs, anti oedematous drugs like alpha chemo trypsine in the 1st 3 days post operative , x-rays were done, the patients discharged from the hospital after sterile dry dressing was done for wound care in the operation theater.

Oral antibiotics and oral analgesics, anti oedematous drugs had been prescribed for the patients for 15 days, and the patients were advised to elevate the affected limb.

Follow up was done in the out-patient clinic (every one month post-operative) in 1st visit removal of surgical suture, care of the wound, new x-rays were done to follow up and to detect the recurrence of the tumor and the state of adjacent joint.

The patient then came every 2 months for another 6 months, then every 3 months for first 2 years, in every visit plain X-rays were done, complete functional examination was performed for the affected limb.

Functional outcome was assessed using musculoskeletal tumor society functional scoring system (MSTS) (**Table 1**). It was done 6 months post-surgery and in the last follow-up.

The patients were examined both clinically and radiologically for detection local recurrence. Following curettage and cementation, normally there was an osteolytic zone caused by thermal injury measuring about 2 mm at cement– bone interface which was bordered by a thin outer sclerotic rim for about 6 months.[12,13] Local recurrence was considered to be present when there was progressive increase of the osteolytic zone more than 5 mm or absence of the sclerotic rim.[14] Recurrence in soft tissues was considered if there was peripheral calcification around a soft tissue mass of uniform density.[5]

Table 1: Functional scoring system of MSTS for the lower limb.[15]

Score	Pain	Function	Emotional acceptance	Supports	Walking Ability	Gait
5	None	No restriction	Enthused	None	Unlimited	Normal
4	Intermediate	Intermediate	Intermediate	Intermediate	Intermediate	Intermediate
3	Modest	Restriction in recreational Activities	Satisfied	Brace	Limited	Minor cosmetic
2	Intermediate	Intermediate	Intermediate	Intermediate	Intermediate	Intermediate
1	Moderate	Partial Disability	Accepts	One cane or crutch	Household	Major cosmetic minor handicap
0	Severe	Total disability	Dislikes	Two canes or crutches	Unable to walk un-aided	Major cosmetic Major handicap

Statistical analysis:

Statistical analysis was performed using IBM SPSS Statistics for Windows, Version 22.0 (IBM Corp., Armonk, NY, USA).

Results

The age of the patients at the time of diagnosis ranged from 24 to 50 years with a mean of 31.55 years ±6.62. Where the period of follow up ranged from 24 to 42 months with a mean of 28.6 months±2.[12].

The mean functional outcome for all patients at final follow up was 28.05±1.099 (93.05%±3.5) with a range: 26-29 (86%-96%). (**Table 2**) represents the characteristics of the patients, the grading, the reconstruction method, the use of internal fixation, complications, functional results and the follow-up period.

Local recurrence occurred in two cases (10%). In the first case, local recurrence occurred after 22 months of surgery and was treated by redo (extended curettage followed by LN as adjuvant and bone cement as filler) (**Fig. 4**). In the second case, local recurrence occurred 26 months after surgery and was treated by wide resection and endoprosthetic replacement **(Fig. 5**). No local recurrence was detected in the remainder of cases till the last follow up.

Limitation of knee range of motion was reported in one case and was managed by physiotherapy for 3 months till full range of motion was achieved.

Two patients with upper tibial tumor resection had common peroneal nerve palsy , one of them improved after 6 months with physiotherapy ,the other one not improved with physiotherapy and refuse to do further interventions.

There was one case of superficial wound infection in the distal tibia, it was improved by administration of parenteral anti biotics for 10 days and oral quinolones for another 10 days.

Table 2: The characteristics of the patients, the grading, the reconstruction method, the use of internal fixation, complications, functional results and the follow-up period (No.: number, M: male, F: female, C: cement, G: graft, IF: internal fixation, ROM: range of motion, #: fracture, F.up: follow up).

No.	Age	Gender	Site	Grade	Reconstruction	IF	Complications	Score	Score (%)	F.up
1	30	F	Proximal tibia	I	C	No	No	29	96	27
2	26	F	Proximal tibia	I	C	No	Recurrence	29	96	35
3	25	F	Proximal tibia	II	C+G	Yes	No	28	93	27
4	25	M	Distal tibia	II	C+G	Yes	Infection	27	90	26
5	28	F	Distal femur	II	C+G	Yes	No	29	96	25
6	35	M	Distal femur	II	C+G	Yes	Recurrence	29	96	42
7	27	F	Distal tibia	I	C	No	No	29	96	27
8	27	M	Proximal tibia	II	C+G	Yes	No	27	90	24
9	40	F	Proximal tibia	I	C	No	No	29	96	26
10	50	F	Distal femur	II	C+G	Yes	Limited ROM+#	27	90	34
11	31	M	Distal femur	III	C+G	Yes	No	29	96	37
12	40	M	Distal femur	II	C+G	Yes	No	29	96	27
13	29	M	Distal femur	II	C+G	Yes	No	29	96	26
14	24	F	Proximal tibia	II	C+G	Yes	Nerve palsy	28	93	27
15	31	F	Distal tibia	II	C	Yes	No	28	93	24
16	32	M	Distal femur	III	C+G	Yes	No	26	86	25
17	34	M	Distal femur	III	C	Yes	No	27	90	24
18	27	F	Distal femur	III	C+G	Yes	No	27	90	32
19	30	F	Proximal tibia	III	C+G	Yes	No	26	86	30
20	40	F	Proximal tibia	III	C	Yes	Nerve palsy	29	96	27

Fig. 4 (A-F): A: Plain X-Ray shows osteolytic lesion affecting the medial tibial condyle, reaching to the subchondral bone. **B**: CT (axial, sagittal and coronal) showed the lesion without cortical breaching. **C:** MRI (axial, sagittal and coronal) showed that the tumour is intraosseous with no soft tissue extension. **D:** Immediate postoperative x-ray. **E and F:** Local recurrence. (**E:** plain x-ray, **F**: MRI).

Fig. 5: local recurrence **(A)** of the tumor that was treated by wide excision and endoprosthetic replacement **(B).**

Discussion

Due to the high rate of recurrence of giant cell tumor after primary surgical excision of the tumor, many procedure had been tried to minimize the rate of recurrence, decreasing of complications and to obtain better functional and oncological results.[16]

In the literature, it had been reported that the rate of local recurrence ranged from 15% to 26%.[8,11,17,18]. While in the current study the recurrence rate was10% (two cases) after 28.6 months as a mean period of follow up.

In the current study, twenty patients with GCT of bone of the lower limb were treated by extended curettage using the high speed burr, LN as an adjuvant, bone cement ±bone graft as filler in all cases. The mean functional outcome for all patients at final follow up was 28.05±1.099 (93.05%±3.5) with a rate of local recurrence. **Table 3**

Table 3 : Comparison between the results of other studies and the results of current study

Study	Number of patient	functional score (mean)	local recurrence	Follow up (mean)
Abdelrahman M. et al[5]	28	93.9%	3.5%	34m
Kafchitsas K. et al[2]	21	92.9%	23.8%	8.7y
Khalil E.A et al[7]	22	94.1%	18%	24m
Gupta A.K. et al[19]	54	90.3%	35%	5y
Muramatsu K. et al[4]	19	88.6%	0%	45m
ES Ng et al[18]	7	92.6%	29%	60m
Yoshinao Oda et al[20]	6	100%	50%	5y
Current study	20	93.05%	10%	28.6m

In trial to find the hidden etiology and the predictive factors which lead to local recurrence of the tumor ,many authors had tried to find the correlation between grading of the tumor and the rate of recurrence, they stated that no direct relationship between the grade of the tumor and the rate of recurrence,[2,11,15,20,25-27] this hypothesis go with the results obtained in this current study where we had two cases of local recurrence one of them was Campanacci grade I and the other was Campanacci grade II, no one was grade III.

On the other hand some authors advocated that the most important factor in prevention and deceasing of the recurrence rate is adequacy of tumor resection which being the most important factor that predicts prognosis.[18,21,22,23]

By introducing the modern technique and technology in treatment of such tumor with high local recurrence rate, and the improvement of recurrence rate with such technique which had followed in this current study, the questions about the cause of improvement in recurrence rate had appeared, is it adjuvant materials, is it curettage, is it cement or burr autogenous graft, or all of them? Or still the adquecy of tumor removal is the corner stone in prevention of recurrence?

Cryosurgery powered the margin of simple curettage make it equal to wide resection as it make tumor cell death 2cm away from the tumor cavity margins, on the other hand bone cement allow heat necrosis to the tumor cells, early rehabilitation and immediate stabilization. [28]

Kafchitsas et al.[2] had reported 52.9% local recurrence rate of 17 patients with GCT treated by curettage only with an average 8.7 years follow up. O'Donnell et al.[29] had reported 33.3% as a rate of local recurrence using curettage and bone cement which decreased to 16.6% combined mechanical burr and bone cement were used. Capanna et al.[30] had published his results of 17% local recurrence rate with the use of different local adjuvants in comparing with 45% recurrence rate with only curettage.

Trieb et al.[31] had gained the same results when he used the curettage with a high speed burr and reconstruction with autogenous graft and use of cement and other adjuvant therapy. He had gone with the adequacy of the tumor resection is the main factor in determining the rate of recurrence. Blackley et al.[32] suggested that the adequacy of the tumor removal was an important factor that determined the risk of recurrence in addition to cement packing.

In the current study, all the patients were treated by extended curettage using large cortical window, the high speed burr, LN as an adjuvant, bone cement in all cases with a rate of local recurrence 10% after a mean follow up period 28.6 months. Our belief is that all these combinations appear to be effective in decrease the rate of local recurrence of giant cell tumor.

Also, a thin layer of autogenous cortico-cancellous iliac bone graft was placed between the exposed subchondral bone and bone cement in 13 cases where most of the stress-bearing articular surface area was affected by curettage. This graft was added to provide a stress-absorbing layer between the articular surface and the bone cement and also to counteract the thermal effect of the cement to prevent the development of later degenerative arthritis. Although degenerative arthritis was not detected in any of our cases, we could not guarantee its future development due to relatively short follow up period. Bini et al[33], had reported 11% of patients had degenerative arthritis using of bone cement in thin subchodral bone. However In the study done by Kaechitsas et al.[2] 87.5% of the patients treated with cement packing after curettage had a good range of motion, they advocated that, there was no relation between cementation and the development of arthritis. on the other hand, In the study done by Lackman et al.[34] Only 1 patient out of 63 had developed osteoarthritis

A further long term study is needed to evaluate the

long-term results regarding the rate of local recurrence, the re-recurrence and the development of degenerative arthritis. Also, a wider scale of cases is needed to extract more significant conclusions.

Conclusion

The use of cryosurgery in combination with curettage with high speed burr together cement packing in treatment of giant cell tumor of bone of lower limb has good functional and oncological results regarding decrease the local recurrence rate, and limits the indications of wide resection.

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