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Clinical results of knee juxta-articular giant-cell tumors treated with bone cement filling and internal fixation after extensive curettage

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Giant cell tumors (GCTs) are benign tumors which exhibit a local invasive behavior and a relatively high rate of recurrence, if treated inappropriately.[1] The reported recurrence rate of simple curettage is approximately 30 to 50%, while it is approximately 7% in patients who undergo with *en-bloc* resection.[2,3] *En-bloc* resection can reduce the recurrence rate, but extensive bone resection often sacrifices joint function.[4] Gitelis et al.[5] obtained similar results and reported that wide *en-bloc* resection could achieve a recurrence rate of 0%, but it also diminished the limb function.

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ABSTRACT

Objectives: This study was to evaluate the radiological and clinical outcomes of patients with juxta-articular giant-cell tumors (GCTs) around the knee treated with bone cement filling and internal fixation after extensive curettage.

Patients and methods: A total of 15 patients (6 males, 9 females; mean age: 35.3±8.4 years; range, 24 to 53 years) with juxta-articular GCTs around the knee were retrospectively reviewed between January 2010 and June 2020. Wound healing, functional status as assessed by the Musculoskeletal Tumor Society (MSTS) scores, local recurrence, metastasis, and complications were evaluated.

Results: The mean follow-up was 41.3±9.9 (range, 24 to 69) months with an overall survival of 93.3%. The mean distance between tumor and cartilage was 6.29±3.73 mm. Five patients underwent reconstruction with cancellous allografts and the mean distance between tumor and cartilage was 2.20±1.48 mm in these patients. At the final follow-up, three patients had Kellgren-Lawrence Grade 2 tibiofemoral osteoarthritis in the operated knee. Lucent zones around the bone cement with no further progression were found in five patients. One patient experienced recurrence 17 months after surgery and was treated by *en-bloc* resection and reconstructed with a tumor endoprosthesis. The remaining 14 patients had a mean MSTS score of 26.86±2.11 (range, 23 to 30) at the final follow-up. The mean overall range of motion at the final follow-up was 109.20±14.20° (range, 85 to 130°).

Conclusion: Bone cement filling and internal fixation after extensive curettage is a viable strategy for accessing juxta-articular GCTs around the knee. The choice of local adjuvants, subchondral bone grafting, and the thickness of subchondral bone require more attention to preserve the continuity of articular cartilage.

Keywords: Bone cement filling, extensive curettage, internal fixation, Juxta-articular giant-cell tumor.

Juxta-articular GCTs around the knee are common and pose a special problem of reconstruction and joint preservation after tumor excision, which often occur predominantly in the patients aged 30 to 40 years.[6,7] The optimal goal is to achieve complete tumor removal and the maximum preservation of joint function. To date, preserved joint reconstruction of juxta-articular GCTs is still a major clinical challenge for surgeons, particularly in patients with extraosseous extension or less subarticular bone. Considering the local aggressiveness of GCTs, the preferred treatment is intralesional extensive curettage with adjunctive procedures. However, there is no consensus about the optimal adjuvants for minimum recurrence. Kivioja et al.[8] analyzed 294 patients with GCTs and suggested intralesional surgery as the first choice for GCTs, even for patients with pathological fractures. Bone cement was preferred for reducing the local recurrence rate. Fraquet et al.[9] reported that cementation could reduce the recurrence rate and provide an excellent mechanical and functional qualities. Previous published studies also have reported similar results.[10] However, there is inconsistency that bone cement is associated with a high rate of secondary osteoarthritis. Some remedies have been attempted to prevent secondary osteoarthritis. Wu et al.[11] used subchondral bone grafting combined with bone cement reconstruction for patients with giant-cell tumors around the knee, and the recurrence rate was 3.7%. However, due to the limited number of cases, there are still insufficient functional outcomes associated with this treatment.

To achieve better joint reconstruction of juxta-articular GCTs around the knee, in the present study, we aimed to evaluate the clinical functional outcomes of bone cement filling and internal fixation after extensive curettage and to assess the presence of secondary arthritis during follow-up.

PATIENTS AND METHODS

Study design and study population

This single-center, retrospective case series was conducted at Changzhou Hospital Affiliated to Nanjing University of Chinese Medicine, Department of Orthopaedics between January 2010 and June 2020. A total of 15 patients (6 males, 9 females; mean age: 35.3±8.4 years; range, 24 to 53 years) with unilateral juxta-articular GCTs around the knee were included. Inclusion criteria were as follows: having tumors located near the joint, new cases without prior management, and pathological diagnosis of GCTs. Patients who underwent total knee arthroplasty or bone resection were excluded. A written informed consent was obtained from each patient. The study protocol was approved by the Ethics Review Committee of Changzhou Traditional Chinese Medical Hospital, affiliated to Nanjing University of Traditional Chinese Medicine. (date: 10.02.2020, no: 2020-LL-012(L)). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Surgical technique

At the initial diagnosis, physical examination, plain radiographs, computed tomography (CT), and magnetic resonance imaging (MRI) were performed to assess tumor growth. Fine-needle percutaneous biopsy was performed to confirm the diagnosis of GCTs, but the biopsy track could be available for resection in future surgery.

All surgeries were performed under general anesthesia by a single experienced surgeon. The patients were placed in the supine position. The surgical approach was designed based on the lesion. After adequate exposure of the tumor, surgical gauze was placed around the tumor to prevent surrounding tissue contamination. A cortical window was opened by Coriolis needle drilling, and the intraosseous tumor tissues were removed completely by a hand-held curette. The amount of removed lesion was based on the extent seen on CT and MRI preoperatively. It is of utmost importance to preserve ligamentous structures to maintain limb function.[12] Radical curettage was performed till the healthy bone margin. A high-speed burr was used to grind the paratumorous bone to enlarge the cavity. The remnant margin was cauterized by an electrotome and, then, denatured by 5% phenol-soaked gauze. The phenol was removed by ravaging with 99% alcohol. The main goal of all these procedures was to achieve radical marginal excision. If leisure destroyed partial articular cartilage, a 0.5-cm thick allograft bone was paved under the surface of cartilage surface to the increase the endurance of the subchondral bone.[13,14] If the tumor extended into soft tissues, all the contaminated surrounding soft tissue and pseudo-capsule could be completely removed. Intraoperative images were taken to confirm a clear margin of intralesional curettage.

Polymethylmethacrylate (PMMA) cementing combined with a plate was chosen for skeletal support. The bone defect was, then, filled with PMMA cement. The plate was placed at the bone defect to provide sufficient mechanical stability before the

cement was about to be set. Next, the wound was sutured in layers after adequate hemostasis.

The rehabilitation regime was tailored based on the individual needs of each patient. If tolerable, the patients were encouraged to perform isometric muscle strength training after surgery. The range of motion (ROM) exercise varied among individuals. A non-weight-bearing stand with two crutches was permitted four weeks after the operation, and the patients gradually transitioned to partial and full weight-bearing stands.

Definitions and outcome measures

The follow-up duration was defined as the interval between the date of the operation and the date of the final visit. Postoperative follow-up included clinical and radiographic assessments at one, three, six, and 12 months and, then, annually thereafter. Chest CT was performed every six months. Physical examination and plain radiographs were needed at each visit to assess failure of cement filling[15] or internal fixation, tumor recurrence, and metastasis.

The radiographic staging system of Campanacci et al.[16] was used to classify GCTs based on their radiographic appearance.

The Musculoskeletal Tumor Society (MSTS) score[17] was employed to evaluate functional outcomes, including pain, functional limitations, walking distance, support use, emotional acceptance, and gait.

Compared to that of the contralateral knee, secondary arthritis was staged using the Kellgren-Lawrence (KL) classification.[18]

The ROM of the knee was measured in the supine position using a goniometer.[19]

The degree of pain was measured by the Visual Analog Scale (VAS). The patients were asked to mark their level of pain on a 10-cm VAS.[20]

Complications, such as infection, local recurrence, fracture and joint narrowing, were also recorded.

Statistical analysis

Statistical analysis was performed using the SPSS version 24.0 software (IBM Corp., Armonk, NY, USA). The distribution of the data was evaluated using the Kolmogorov-Smirnov test. Continuous variables were expressed in mean ± standard deviation (SD) or median and interquartile range (IQR), while categorical variables were expressed in number or frequency.

RESULTS

Table I shows baseline characteristics of the patients. The mean follow-up was 41.3±9.9 (range, 24 to 69) months with an overall survival of 93.3%. Five of 15 patients underwent reconstruction with

TABLE I
Baseline characteristics of patients

No	Age/Sex	Laterality	Campanacci radiographic system	Surgical time (min)	Complication	Follow-up time (m)	MSTS	Recurrence	Metastasis
1	26/F	R	II	90	None	35	23	None	None
2	24/M	L	I	90	None	24	28	None	None
3	38/F	R	II	80	DWH	39	27	None	None
4	30/F	L	I	80	None	40	20	Yes	None
5	41/M	R	III	110	None	69	25	None	None
6	26/F	L	II	90	None	36	27	None	None
7	30/M	R	II	85	None	34	30	None	None
8	32/F	R	I	90	Pain	42	28	None	None
9	29/M	L	II	90	None	48	28	None	None
10	37/F	R	II	90	None	40	25	None	None
11	36/M	L	I	90	None	45	29	None	None
12	38/F	R	II	100	None	50	30	None	None
13	53/F	L	II	90	DWH	36	26	None	None
14	42/F	R	II	105	None	43	25	None	None
15	49/M	R	II	100	None	38	25	None	None

MSTS: Musculoskeletal Tumor Society; L: Left; R: Right; DWH: Delayed wound healing.

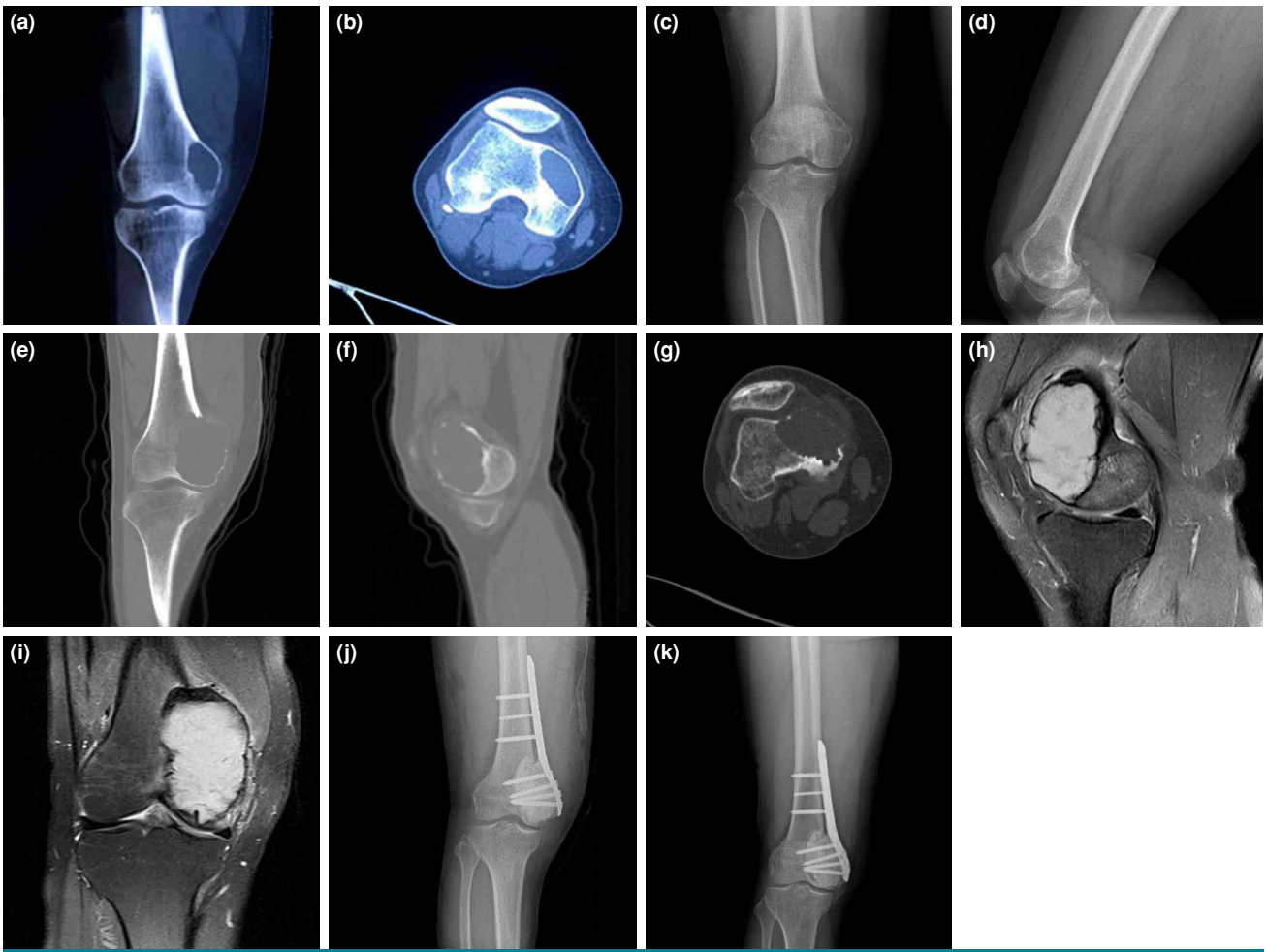

FIGURE 1. A 41-year-old man with the knee juxta-articular giant-cell tumor, complaining pain in the right knee for nine months. **(a, b)** The initial CT examination showed bone destruction lesion with sclerotic margin and misdiagnosed as bone cyst at the first visit hospital. **(c-i)** About nine months later, an expansile radiolytic lesion with non-sclerotic margin was found in medial femoral condyle in the plain film. CT and MRI confirmed the hyperintense lesion in the epimetaphyseal region of medial femoral condyle. Some lesions destroyed partial articular cartilage and bulged into soft tissue. **(j)** the postoperative plain film showed preserved joint reconstruction with bone cement filling and internal fixation. **(k)** After five years postoperatively, the plain film showed no signs of recurrence. Lucent zones around the bone cement with no further progression was found.
CT: Computed tomography; MRI: Magnetic resonance imaging.

cancellous allografts and mean distance between the tumor and cartilage was 2.20±1.48 mm.

According to the Campanacci et al.'s.[16] classification, four patients had Grade 1, 10 had Grade 2, and one had Grade 3 GCTs.

All patients resumed their daily life and jobs pain-free (Figure 1). Thirteen of 15 patients could walk without any aid at the final follow-up. One patient experienced recurrence 17 months after surgery and was treated by *en-bloc* resection and reconstructed with a knee joint tumor prosthesis. It had the lowest MSTS score (23 points). The remaining 14 patients had a mean MSTS score of approximately 27.07±1.82 (range, 25 to 30) at the final follow-up. For all patients, the mean ROM at the final follow-up was 109.20±14.20° (range, 85 to 130°). Twelve of 15 patients could extend completely and flex more than 100°, and three patients could extend completely but flex no more than 90°.

None of the patients had signs of knee OA according to preoperative X-ray, and all the contralateral knees had no signs of OA (KL-0 or KL-1) at the final follow-up. The mean distance between the tumor and cartilage was 6.29±3.73 mm. Lucent zones around the bone cement with no further

progression were found in five patients. At the final follow-up, three patients had KL Grade 2 tibiofemoral OA in the operated knee. Of them, two patients underwent reconstruction with cancellous allografts. The distance between tumor-cartilage was 0, 2, and 7, mm respectively.

No serious complications such as failure of internal fixation, deep infection, or fracture occurred in any patients. Two patients experienced delayed wound healing after dressing changes. One patient complained of pain which was relieved after oral painkillers.

DISCUSSION

The management of juxta-articular GCTs around the knee remains a major clinical challenge for surgeons to maintain native joint function with minimum recurrence. In the present study, we showed that bone cement filling and internal fixation after extensive curettage was a viable strategy for accessing juxta-articular GCTs around the knee. The continuity of articular cartilage was a key factor contributing to degenerative arthritis. Therefore, more attention needs to be given to subchondral bone grafting and the thickness of subchondral bone to restore the continuity of articular cartilage.

It is challenging to achieve complete removal of the tumor in the cavity. Local adjuvants are used to destroy microscopic tumor foci and minimize the recurrence rate. Adjuvant treatment followed by curettage could prevent morbidities associated with decreased recurrence.[21]

Many physical and chemical methods have been used to effectively remove tumor tissues and decrease local recurrence after curettage. Algawahmed et al.[22] proposed that a high-speed burr was an effective method for reducing the local recurrence rate. Intralesional curettage with high-speed burring results in a low recurrence rate of approximately 12 to 25%.[22] Electrocautery can destroy tumor cells beyond 6 mm and provides a relatively safe margin.[23] Chemical adjuvants include phenol, alcohol, hydrogen peroxide, and liquid nitrogen.[24] As a local adjuvant, phenol must be used with great care to protect soft tissues. It could improve local control by chemical burns on the surgical margin.[25] In the present study, a high-speed bur, an electrotome and phenol were combined to achieve radical marginal excision. In contrast, Blackley et al.[26] proposed that adequate removal of tumor tissues was a key step for reducing local recurrence, but was not related to adjuvant modalities. Ruggieri et al.[27] also analyzed the effects of different local adjuvants and proposed that any local adjuvant did not reduce recurrence, but increased the rate of complications.

A meta-analysis investigating the efficacy of bone cementation and allogeneic bone grafting suggested that adjuvant bone cementation was preferable with lower local recurrence.[28] The polymerizing heat during bone cement solidification can reach 80 to 90°C, and the heat penetration during the setting of the cement is approximately 3 mm in depth. The exothermic reaction of PMMA can kill local remaining tumor cells to reduce recurrence.[29,30] Bone cement can easily fill irregular defects at a relatively low cost. Bone cement filling immediately reconstructs bone defects and exhibits good mechanical strength for early weight-bearing.[31] Subchondral bone replaced by cement can alter the biomechanics, but does not influence knee function or quality of life. It helps the subchondral stiffness recover to 98% of that of the healthy limb.[32]

In our center, PMMA cementing combined with a plate was chosen for skeletal support after adjuvant treatments. All patients were followed for a mean of 41.27±9.90 months with an overall survival of 93.3%.[33] Previous studies have confirmed similar results. The combined use of the burr down technique, phenolization and polymethyl methacrylate is a safe method with a reduced local recurrence of 5.1%.[34] Satisfactory functional results can also be achieved when GCTs are treated with intralesional curettage with high-speed burr, electrocauterization and bone cement. A tumor with a large soft tissue extension usually increases the risk of local recurrence.[35] We also added other adjuvants to widen surgical margins to reduce recurrence.

Little is known about the risk factors for degenerative changes. Wada et al.[36] reported that the continuity of articular cartilage was the main factor contributing to degenerative arthritis. If the continuity of the articular cartilage is preserved, intralesional curettage with cement filling does not increase the rates of recurrence or degenerative osteoarthritis.[37] The incidence of secondary osteoarthritis is low after a median follow-up period of 131 months.[38] Therefore, more attention is needed to protect the articular cartilage during surgery. Some researchers are concerned that the high polymerization temperature may be harmful to cartilage. In the present study, no serious degenerative changes were found. This finding

indicates that concerns about secondary arthritis may be superfluous. However, concern about the increased risk of long-term degenerative changes still exists due to the weight-bearing nature of bone cement.[11]

Some authors have shown that bone cement results in further damage to subchondral bone. To prevent thermal damage to articular cartilage, subchondral bone grafting is used to reduce secondary osteoarthritis. The allograft was paved under the surface of the cartilage surface to increase the endurance of the subchondral bone and prevent heat necrosis. Suzuki et al.[39] reported that the incidence of second osteoarthritis was only 11% after the combination of PMMA and subchondral cancellous bone graft. Allogeneic bone grafting is a widely accepted method for filling lesions under the articular surface. To maintain the disrupted articular cartilage, we interposed bone chips under the cartilage to prevent harm from the cement. The interposed chips could maintain the joint shape with better functional results. The distance between the tumor and cartilage and the area taken up by the tumor were the main risk factors for developing OA. Van der Heijden et al.[40] reported the similar results and proposed that the risk of OA increased 4.2 times, if the remaining subchondral bone was less than 3 mm. Currently, there is no consensus about the relation of thickness of remaining healthy subchondral bone and arthrosis. In contrast, Caubère et al.[41] conducted a study of patients with GCTs in the knee area treated by curettage-cement packing. They concluded that the small quantity of subchondral bone remaining after curettage was correlated with the development of knee OA. However, replacing subchondral bone with cement did not affect the functional outcomes or quality of life.

Cementation offered immediate stability for earlier weight bearing with less morbidity.[42] Another study showed that bone cement also reduced the relapse rate after surgery.[8] In present study, a plate was used to provide early stability and control the micro-motion between the cement and bone. The composite fixation of bone cement and internal fixation provides sufficient stability to reduce subsequent postoperative fracture and reconstruction failure. Similarly, Yu et al.[43] suggested that oral bisphosphonates were also needed after patients treated with aggressive curettage, cement filling and internal fixation. However, there is still a lack of sufficient evidence regarding the benefits of additional oral bisphosphonates.[43]

The loss of appropriate cortical bone may increase the risk of fracture. During the preoperative plan, it is a key step to prepare materials with potential for residual defects after intralesional curettage. Bone cement combined with internal fixation exhibited better biomechanical strength than that of bone cement alone.[44] In addition, internal fixation is needed to avoid further stress-induced resorption of bone around the cement.[45] The radiolucent zone is believed to be associated with thermal injury of bone cement fillings. In present study, radiolucent zones at the bone-cement interface existed in most patients, but they were non-progressive. The progressive osteolysis of the radiolucent lines may result in gross loosening.

Nonetheless, there are several limitations to this case series. First, it has a retrospective design with a small sample size. Second, it has a relatively short follow-up and long-term follow-up is needed to definitively evaluate the prognosis including recurrence and joint degeneration. Third, we used the Campanacci system which is solely based on interpretation of complex morphologies in two-dimensional radiographs and in which identification of tumor borders precisely is difficult.[46] This may have led to a potential observer bias. Further multi-center, large-scale, long-term prospective studies are needed to evaluate the effects of different adjuvant methods.

In conclusion, bone cement filling and internal fixation after extensive curettage provide a fine joint function. However, to preserve the continuity of articular cartilage, some issues still require attention, including the choice of local adjuvants, subchondral bone grafting and the thickness of subchondral bone.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions: Wrote the main manuscript: L.M., C.J.; Undertook data management and statistical analysis: X.Z., G.M.; Contributed to data management and literatures review: G.B., W.Y.; Designed the study and managed overall process: X.J., Z.J. All authors have approved the final manuscript.

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