

Oncological and functional results following operation for giant cell tumour of bone

Yongzhong Wei^{a,*}, Eugene T.H. Ek^b, Lipeng Yu^a, Guoyong Yin^a

^aDepartment of Orthopedics, The First Affiliated Hospital of Nanjing Medical University, Nanjing, 210029, China

^bDepartment of Orthopaedics, St Vincent's Hospital Melbourne, Australia

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Abstract

Objective: Giant cell tumours (GCT) represent one of the most common benign tumours of bone. However, despite its benign nature they are aggressive lesions that have a tendency to recur. This study aims to report experience with the treatment of GCTs, and reviews the relationship between surgical management and clinical outcome. **Methods:** A retrospective review was performed with 70 patients (32 males and 38 females) who presented to our institution between 1991 and 2001 with GCT of bone. An evaluation of the oncological and functional results was conducted and patients were divided into three groups according to the treatment method; Group I (46 patients) intralesional curettage and adjuvant therapy and packing with filling materials. Group II (18 patients) en-bloc resection and arthrodesis or reconstruction. Group III (6 patients) amputation. **Results:** The mean follow-up period was 10 years (range, 5–15 years). The overall rate of local recurrence was 14%, 22% in Group I, and only 4% in Group II and Group III. According to the Musculoskeletal Tumour Society (MSTS) score for functional outcome, the mean overall score for Group I was 27.9 (out of 30), 15.9 for Group II. Of note, the 9 patients within Group II who received endoprosthetic reconstruction, the mean overall MSTS functional score was 25.5. **Conclusion:** Intralesional curettage with adjuvant therapies and filling agents is often associated with a relatively high recurrence rate, however joint function is well preserved. Patients with more extensive, biologically aggressive, and/or recurrent tumours are best treated with en-bloc resection.

Key words: giant-cell tumour of bone; treatment; recurrence; outcomes

INTRODUCTION

Giant cell tumour (GCT) of bone represents one of the most common primary tumours of bone^[1]. Although generally classified as benign lesions, GCTs are locally aggressive tumours that commonly arise in the epiphyseal region of long bones. To date, the histogenesis of GCT is still relatively unclear and its clinical behavior and prognosis is difficult to predict from histopathological features.

The ideal form of treatment for these lesions (in particular those that arise near major joints) remains controversial. As such, there are a variety of surgical options ranging from intralesional curettage (with or

without adjuvant agents) to *en bloc* or wide resection with reconstruction. As with all bone tumours, the primary objective of treatment of giant cell tumours is to eradicate the tumour tissue, reconstruct the bone defect, and restore limb function. Historically, patients who had intralesional excision had improved functional results, however tumour recurrence rates were in the range of 30–50%^[2,3]. As a result, this has led to the use of adjuvant agents to decrease the recurrence rates^[4–8]. On the other hand, some authors have reported that *en bloc* resection results in lower recurrence rates, however this is at the expense of functional outcome when compared to intralesional excision^[9].

The purpose of this study is to describe our experience with the surgical management of GCTs and to analyze the effects of different forms of treatment on local recurrence rates and clinical and functional outcome.

*Correspondence author.

E-mail address: wyz202@hotmail.com

PATIENTS AND METHODS

A retrospective analysis was performed of all patients that presented to the authors institution between 1991 and 2001 with GCT of bone. At the time of initial presentation and at latest follow up, all patients had plain radiographs of the lesion and chest films. Computed tomography(CT) and magnetic resonance imaging (MRI) scans were used to assess tumour location and size, adequacy of initial treatment and site of recurrence in the part of patients.

According to the grading system of Campanacci^[10], 14 lesions were classified as Grade I, 37 were Grade II, and 19 were Grade III. As per our institution's protocol, if the clinical and radiological presentation was characteristic of a benign GCT, biopsy and surgery were performed at the same session. If the presentation was atypical, open incisional biopsy was performed and further surgery was delayed until the histological evaluation had been completed.

Patients were divided into three groups: Group I (46 patients; 14 Grade I, 32 Grade II) contained those treated with intralesional curettage and adjuvant local treatment and filling agents, such as the use of phenol or zinc chloride and bone grafting (autograft and/or allograft). Group II (18 patients; 6 Grade II, 12 Grade III) comprised of those that were managed with *en bloc* or wide resection with reconstruction using large structural bone grafts to fill the defects or endoprostheses. Reconstruction was individualized according to the age of the patient, the location of the tumour, the functional demands and the preference of the patient. Both the fibula and the iliac crest were used as large vascularized bone segments. Of the 18 patients (2 in the distal radius and 1 in proximal tibia) a vascularized bone was required for the reconstruction of a new articulating surface. Six patients with tumours arising from the distal femur in four, and proximal tibia in two underwent arthrodesis. Nine patients had resection and endoprosthetic reconstruction: 6 in distal femur, 1 in proximal tibia, and 2 in proximal humerus. In all cases, a continuous passive motion(CPM) machine has been applied post-operatively and maintained until discharge. Group III (6 patients; 6 Grade III) included patients who had undergone amputation due to extensive local destruction by the tumour and/or involvement of blood vessels or nerves(**Fig 1**).

Local recurrence was determined clinically, radiologically, and pathologically. Functional analysis was performed at the time of latest follow-up visit. Functional evaluation of 51 patients was performed according to the most recent scoring system of the Musculoskeletal Tumour Society(MSTS)^[11]. All scores were added to obtain the overall functional score and expressed as percentage ratings of a normal total score of 30. The

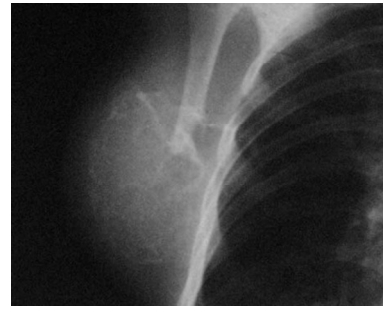


Fig 1 Radiographs showing GCT in the distal part of the humerus

ROM was measured and recorded as a percentage of the full range at that joint. Any flexion deformities or extensor lags or changes in arc of motion specifically were documented.

Statistical analysis

Standard tests(the chi-square test, Mann-Whitney U test, and Fisher exact test) were used to analyze the data statistically. The level of significance was $P < 0.05$.

RESULTS

There were 32 men(45.7%) and 38 women(54.3%) and the mean age at the time of diagnosis was 36 years (range, 11-62). Of the 70 GCTs, 26(37%) were located in the distal femur, 20(29%) in the proximal tibia, 5 (7%) in the proximal femur, 5(7%) in the proximal humerus, 3(4%) in the distal radius, 3(4%) in the sacrum, 2(3%) in the ilium, 1(1%) in the talus, 1(1%) in a metacarpal joint, 1(1%) in the distal tibia, 1(1%) in the fibular head, 1(1%) in the patella and 1(1%) in the distal humerus. In Group I, 4 patients developed post-operative infections, and 3 patients re-presented with a closed pathological fracture. In the Group II, only 1 patient developed aseptic loosening at 5 years post index surgery. The mean follow-up period was 10 years (range, 5-15 years).

The overall rate of local recurrence was 14%. The timing of recurrence ranged from 5 months to 14 years. Seven patients(68%) recurred within three years after their primary operation. Three patients(32%) recurred after four years since operation. Of the three patients, one patient subsequently developed pulmonary metastases. In Group I, the rate of local recurrence was 22%(10 patients). No statistical difference was found between the rate of recurrence and age, gender and use of adjuvant therapies. All patients re-presented with increasing local pain and radiographic features of a well-defined cystic lesion in the area that was previously reconstructed with the bone grafting. Five patients recurred in the distal femur, three in the proximal tibia and one in the proximal femur and one in the proximal humerus. Subsequent treatment of the local recurrence was *en-bloc* excision and reconstruction with an

endoprosthesis in three patients, bone grafting in two patients and amputation in the remaining five patients. In Group II and Group III, the rate of local recurrence was 4% (1 patient). This patient presented with a pathological fracture through a local recurrence in the proximal tibia 10 years post *en-bloc* resection and an osteoarticular allograft. The patient was treated by amputation.

At the time of latest follow up, functional evaluation was not available for 19 patients: 6 patients who had undergone amputation and therefore non-ambulant, 3 patients who suffered from the sacrum tumours, 1 patient who had died from multiple lung metastasis due to malignant transformation of the primary tumour and 9 patients who were unable to visit our clinic for unknown reasons. The mean overall MSTS functional score for Group I was 27.9 out of 30 points (93%). Range of motion was maintained long-term with median knee extension of 0° (range, 0-10° and a median maximum flexion of 110° degrees (range, 55-130°). The mean ROM at final follow-up was 97% (± 2%) at the joint closest to the surgical intervention. The mean overall MSTS functional score for Group Group II was 15.9 out of 30 points, but 9 in the distal femur, proximal femur, proximal tibia and proximal humerus received endoprosthetic reconstruction. The mean overall MSTS functional score was 25.5 out of 30 points.

For the distal radius tumours, excellent bone graft incorporation was observed and satisfactory joint motion was achieved in all of the patients. In the long follow-up periods of 5 to 15 years, there were no radiologic signs of joint degeneration. However, a poor result was noted in terms of functional outcome in 6 patients who received joint arthrodesis. Of the patients with reconstruction around the knee joint, 4 experienced stiffness of the knee with poor range of motion (<20°).

DISCUSSION

GCTs most commonly arise in the distal femur and proximal tibia. In our series, 66% of cases were located within these areas. Although Jaffe^[12] graded these tumours according to histological grade, no correlation has been found between the tumour aggressiveness and the histologic grade^[13,14]. On the other hand, the grading system proposed by Campanacci, which is based on plain radiographic features, has been reported, by many authors, to correlate with risk of recurrence^[15,16]. Therefore, on this basis, the grade of the tumour plays a role in guiding the surgeon in the choice of treatment strategy. In our series, we treated Grade III tumours aggressively with *en-bloc* resection and reconstruction or amputation. In this group of patients, there was only one patient who developed a local recurrence.

The treatment of choice in most Grade I and II GCTs has been intralesion curettage, as this offers a high like-

lihood of cure with a good functional outcome^[5,17]. Historically, however, curettage alone has been associated with a high rate of recurrence (30% to 50%)^[2,3] and therefore various adjuvant therapies (including phenol, zinc chloride, polymethyl methacrylate, liquid nitrogen, and alcohol) may be employed in conjunction with curettage and probably reduce the risk of recurrence compared with curettage alone^[4-8]. Prosser *et al*^[16] reported that the recurrence rate for patients with Grade I and II GCTs was 7%. However, in any series with a predominance of patients with low-Grade tumours it might be expected that good results will be achieved with any treatment, with or without adjuvant therapies.

In our series, patients in Group II received adjuvant therapies (phenol or zinc chloride) and filling agents (bone grafts). We did not observe any significant difference in the recurrence rate when using phenol or zinc chloride. Bone graft with autograft or allograft has been the traditional standard agent for filling defects after curettage of benign bone tumours. Some authors have filled the defect after curettage with bone grafts, autograft or allograft^[18]. Although autograft has the biological advantages of osteoinduction and eventual incorporation to produce a better long-term biologic construct, there is the potential for complications such as donor site morbidity, infection, and graft failure. Although we did experience any donor site morbidity, 4 patients had infection and 3 patients developed pathological fracture.

Good results have been published recently of the use of high-pressure pulsatile lavage and a high-speed burr, which allows the surgeon to remove the contaminated margin up to normal bone^[19,20]. Blackley *et al*^[19] showed, using a high-speed burr at the time of curettage and bone grafting, an acceptable rate of recurrence of 12% in 59 patients. In most benign aggressive bone tumours control can be achieved by wide surgical excision. Following *en-bloc* resection, the rate of the recurrence has been reported to be between 0% and 5% in primary lesions^[21,22]. In our series, only one patient developed local recurrence. Because it is found in the epiphysis, the GCT often invades the subchondral bone. *En-bloc* resection usually requires sacrifice of the articular surface and a complex reconstruction procedure, which can lead to complications, revision operations, and decreased quality of life in the long term. Grade III tumours which have already destroyed the cortex tend to recur more often and when the defect is large and the joint surface destroyed, resection is indicated. In our series, 6 patients had large Grade III tumours that involved blood vessels or nerves, hence necessitating amputation.

Osteoarticular allografts and arthrodeses with autogenous tissue were introduced as limb-sparing

procedures. Donati *et al*^[20] analysing the data of 92 patients with knee arthrodesis concluded that knee resection arthrodesis with allograft implantation is a difficult procedure with a high complication rate. Fracture, infection, and nonunion rates reduce the likelihood of a successful outcome and coupled with the disabilities associated with an immovable knee make this procedure unattractive. In our series, 6 patients with GCT in the distal femur and proximal tibia received arthrodesis, and 1 patient recurred ten years after operation. In addition, the poor functional evaluation involved those patients. As a result, for Grade III and some Grade II tumours, we treated them with en-bloc resection and endoprosthetic reconstruction. In these patients, no recurrences have been seen. Bickels *et al*^[23] reported in 110 consecutive patients (including 8 GCT patients) who had distal femur resection and endoprosthetic reconstruction with a follow up of a minimum of 2 years that function was estimated to be good or excellent in 94 patients (85.4%), moderate in nine patients (8.2%), and poor in seven patients (6.4%). Therefore, distal femur endoprosthetic reconstruction is a safe and reliable technique of functional limb sparing that provides good function and local tumour control in most patients.

The management of local recurrence of GCT varies. Some recommend wide excision for any recurrent lesions, whereas others believe that repeated intralesional surgery with adjuvants for the second or third recurrence is justified^[24,25]. In our series, patients with local recurrence underwent *en-bloc* resection and reconstruction or amputation. As a result, we believe that the most significant factor in reducing recurrence of GCT is the surgical procedure employed for removal of the tumour. Recurrence of GCT is not fatal in most cases, but can lead to disability and a poor quality of life.

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