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ORIGINAL STUDY

Aggressive treatment of giant cell tumour with multiple local adjuvants

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The results of aggressive management of giant cell tumour including high speed burr, argon plasma cauterisation and phenolisation were reviewed. Twenty four patients with primary or recurrent tumours were treated with a standardised protocol. There were 14 women (56%) and 10 men (44%) with a mean age of 34 years (14 to 62). The defects created after curettage and local adjuvants were reconstructed with PMMA. Additionally, internal fixation was used in weight-bearing bones. Local recurrence occurred in only one patient. Two patients (8%) developed pulmonary metastases. Reconstruction failed only in one patient. These findings support that the combined use of local adjuvants in the treatment of giant cell tumour is a safe and effective way to reduce the rate of local recurrence.

Keywords : giant cell tumour ; local adjuvant ; bone tumour ; argon plasma cauterisation.

INTRODUCTION

Giant-cell tumour (GCT) accounts for 5% of all primary tumours of bone. It is a benign but locally aggressive neoplasm which frequently presents as an epiphysiometaphyseal lesion. One of the main objectives of the treatment is to minimise local recurrence. The current trend in the treatment of giant cell tumour is towards joint sparing surgery, which is facilitated by intralesional curettage versus wide resection. Historically, simple curettage was associated with high rates of recurrence because of incomplete removal of the tumour (*16,18*). The combination of extended curettage using a high speed burr, and utilisation of other physical or chemical local adjuvants has been demonstrated to reduce recurrence rates considerably (*2,3,9,11,14*). Successful results were also reported for recurrent tumours or with pathological fractures. Various agents are being used including phenol, liquid nitrogen, hydrogen peroxide, zinc chloride and recently argon plasma cauterisation (APC) (*10*). APC is a novel therapeutic modality of non-contact electrocoagulation that applies high-frequency current by means of ionised argon gas. In comparison to conventional electrocauterisation, APC allows for more controlled coagulation of larger areas with greater uniformity of depth and provides better haemostasis (*12*).

This study evaluates the results of an aggressive approach in treatment of giant cell tumour of bone including high speed burr, argon plasma cauterisation, high concentration of phenol and polymethylmethacrylate.

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PATIENTS AND METHODS

Between 2002 and 2007, 24 patients (25 tumours) with histologically proven GCT were treated with a customised protocol including curettage, high-speed burr, argon plasma cauterisation and phenol. The defect created after curettage was reconstructed with PMMA. There were 14 women (56%) and 10 men (44%) with a mean age of 34 years (range : 14 to 62). Twenty one patients presented with primary tumours and the other three patients were referred with recurrent tumours following previous surgeries. One patient presented with a pathological fracture. Patients with axial lesions, and those with lesions of the appendicular skeleton that required resection due to extensive bone loss or soft tissue extension were excluded from the study.

All patients were evaluated preoperatively by plain radiography, computed tomography (CT), or magnetic resonance imaging (MRI) of the involved extremity and were graded according to the system described by Enneking *(6)*. Of the 25 tumours, 2 lesions were grade I (8%), 6 (24%) were grade II, and 17 (68%) were grade III. Additionally, chest CT was obtained to check for the presence of lung metastasis. Fifteen tumours arose around the knee joint (8 in the distal femur, 6 in the proximal tibia and 1 in the patella). The remaining 10 tumours were located at various epiphysiometaphyseal regions. All of the patients presented with local tumour only and were not metastatic.

Surgical technique

A standardised surgical technique performed by a single surgeon was used in all cases. Following adequate exposure, a large cortical window was created to allow visualisation of the entire lesion. If the tumour extended beyond the cortex, marginal resection was performed through the pseudocapsule of the tumour down to bone. The tumour tissue was removed by curettage including use of a high speed burr. The cavity was then irrigated and dried. The argon plasma coagulator (Force Argon II, Valleylab Boulder, CO, USA) was set at120 watts and applied to the entire cavity until all bone surfaces coagulated. The coagulum on the bone surface was removed with curettes. A 90% phenol solution was then applied on the walls of the cavity with mini sponges. To avoid soft tissue leakage, phenol was not painted on areas where the cortex was perforated. The cavity was then irrigated, first with alcohol then with copious amounts of saline. The bone defect was packed with PMMA. If subchondral bone was exposed by the tumour or during extended curettage, a layer of cancellous allograft was first impacted to protect the joint cartilage from thermal injury due to PMMA. Additionally, structural augmentation was applied with MRI-compatible titanium screws or plates if necessary (fig 1). Postoperatively, patients were started on range of motion and strengthening exercises. Mobilisation with weight bearing was allowed as tolerated.

Patients were followed at three months intervals for the first two years and then at six months intervals up to the fifth postoperative year. Mean follow-up was 33.7 months (range : 14 to 70). Complete physical examinations, as well as plain radiographs and MRI of the affected area were obtained to evaluate any local complications including recurrence, infection, failure of reconstruction and degenerative arthritis of the adjacent joint. Chest CT scans were obtained every six months for the first two years, and then annually for up to a total of 5 years, looking for any possible metastases. Functional evaluation was assessed using the Musculoskeletal Tumour Society (MSTS) grading system *(7)*.

RESULTS

Local recurrence occurred in only one patient with proximal tibia GCT, nine months after the operation. This patient was subsequently treated with wide resection and knee arthrodesis and remained tumour-free at final follow-up, 26 months after the second operation. Two patients (8%) developed pulmonary metastases. The first patient had been referred to the author's institution following two failed surgeries. She developed metastasis 26 months after her third operation. She underwent resection of a single metastatic nodule. She remained disease free after two years. The other patient had a primary tumour at presentation. He developed multiple lung metastases 13 months after surgery. Chemotherapy was started as he had multiple pulmonary nodules ; he is still under treatment. No local recurrence was seen in these patients.

In twelve patients (50%) who were at risk for a fracture due to extensive cortical destruction or a large tumoral cavity, a structural augmentation was performed with screws or plates. Additionally, the patient with a pathological fracture was treated with double plate fixation after curettage and adjuvants. This patient received fractionated radiotherapy for a total of 4000 cGy, starting eight weeks after

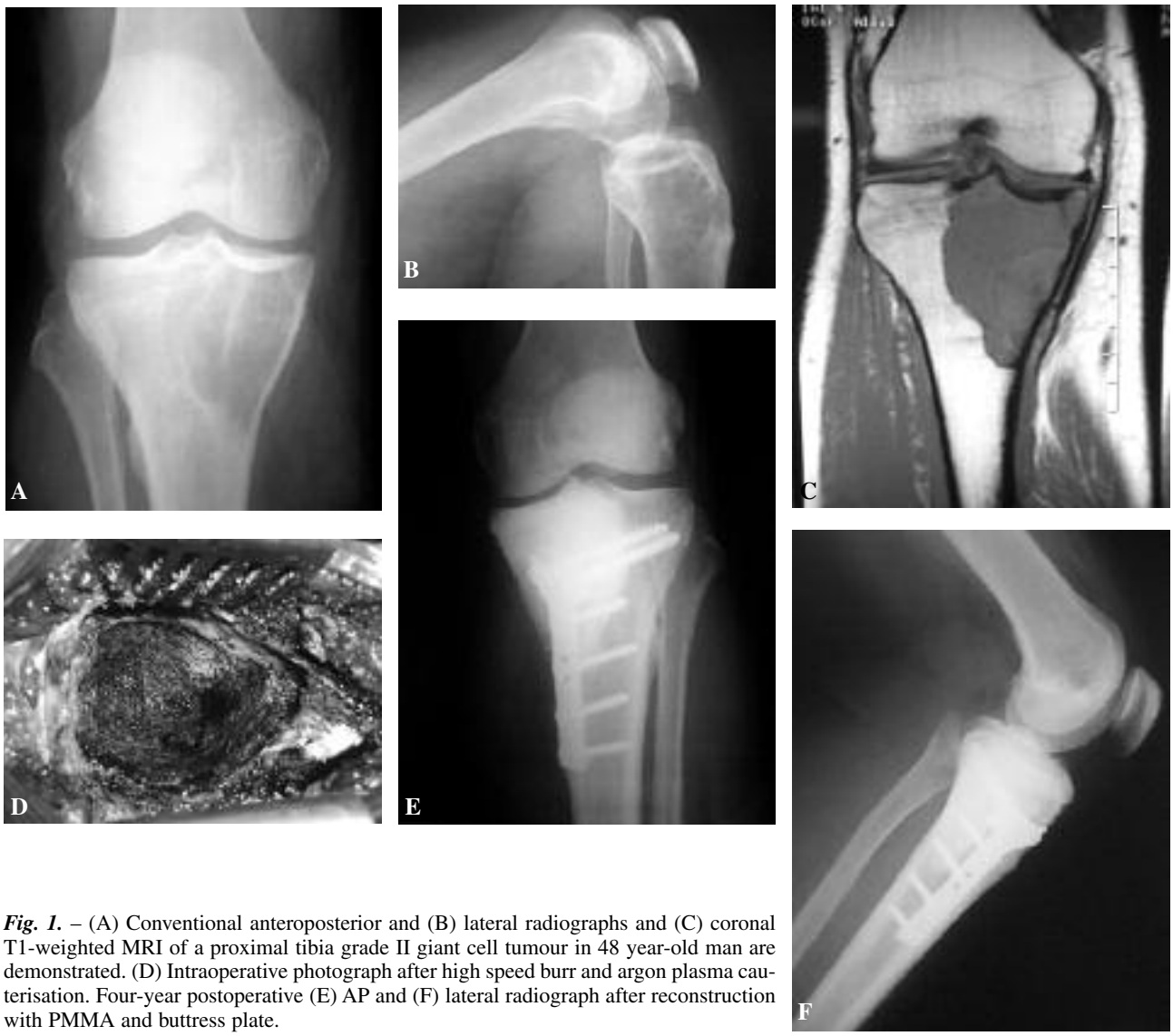

Fig. 1. – (A) Conventional anteroposterior and (B) lateral radiographs and (C) coronal T1-weighted MRI of a proximal tibia grade II giant cell tumour in 48 year-old man are demonstrated. (D) Intraoperative photograph after high speed burr and argon plasma cauterisation. Four-year postoperative (E) AP and (F) lateral radiograph after reconstruction with PMMA and buttress plate.

surgery. The fracture healed uneventfully and he remained disease free 2 ½ years after surgery.

Failure of reconstruction was seen in only one patient, in which the tibial joint surface collapsed after curettage and reconstruction with PMMA and a buttress plate. He was treated with prosthetic replacement.

Joint sparing treatment was possible in all but two patients. The ROM of the adjacent joint was 94% of the unaffected side in the other 22 patients. Three patients has mild (less than 10°) extension lag of the knee. The patient who presented with a pathological fracture and received radiotherapy after surgery had the lowest ROM, with a 10° flexion contracture and 80° of flexion.

The mean MSTS functional score for the upper extremity was 26.3 (range : 16 to 30) corresponding to 87.6% of normal upper extremity function. The mean MSTS score for the lower extremity was 27.9 (range : 21 to 30) corresponding to 93% of normal lower extremity function.

There was no inadvertent damage to adjacent structures due to argon plasma cauterisation or phenol. No systemic adverse effect was observed either. Three patients had delayed wound healing but recovered uneventfully. One patient developed

Table I. — Recent reports of giant cell tumours treated by extended curettage and local adjuvants

Study	Number of patients	Local adjuvant	Filling material	Mean Follow-up (years)	Local recurrence (%)
Zhen *et al* (*23*)	92	50% Zinc Oxide	PMMA	11	13
Blackley *et al* (*3*)	59	None	BG	6.6	12
Lackman *et al* (*9*)	63	90 % Phenol	PMMA	10	6
Saiz *et al* (*15*)	40	12.5% Phenol	PMMA	76	12.5
Bini *et al* (*2*)	38	3% Hydrogen Peroxide	PMMA	5.2	8
Lewis *et al* (*11*)	37	APC	PMMA	6	8.3
Malawer *et al* (*14*)	102	Liquid Nitrogen	PMMA/BG	6.5	7.9
Current series	24	APC+ 90% Phenol	PMMA	3	4

(APC = argon plasma cauterisation ; PMMA = polymethylmethacrylate ; BG = bone grafting).

osteoarthritis. No neurological or vascular injury was seen. No infection was observed in our series.

DISCUSSION

The main determinant in the success of treatment of GCT is complete eradication of the lesion. To achieve this goal, the tumoral cavity is fully exposed through a large cortical window and all the septa are removed with straight and angled curettes, followed by high-speed burring to extend the curettage. Local adjuvants are then applied to the bony walls of the cavity to induce necrosis of any residual tumour cells. Electrocauterisation, phenol and liquid nitrogen are widely used. As a result, the recurrence rates have decreased dramatically in the last two decades (table I). In this study, all the patients were treated by extended curettage followed by argon plasma cauterisation. The cavity was then painted with high concentration phenol. The defect was reconstructed by PMMA and augmented by plates or screws in weight bearing bones. These steps were strictly followed in all the cases. This locally aggressive approach resulted in fairly low rates of recurrence and complications.

As compared with standard electrocauterisation, argon plasma coagulation provides more homogenous and better controlled cauterisation. Since GCT is a vascular lesion APC further helps to control bleeding especially in areas in which a tourniquet cannot be used. Although the use of APC in orthopaedic oncology has been increasing, there is only one study that reports its use in treatment of GCT. Lewis *et al* (*11*) treated 37 patients with GCT with extended curettage, APC and PMMA packing. Tumours recurred in 10.2% of their patients at an average of 18 months. Postoperative complications were seen in 27% of the 37 patients including fractures, deep infection or cellulitis, nerve palsy and tendon rupture.

Phenol has a direct cytotoxic effect by protein denaturation and suppression of cell membrane permeability. It can destroy up to 1-2 mm of tumour tissue by coagulation necrosis (*12*). Many studies showed that the use of phenol has significantly reduced the recurrence rate (*5,9,15,16*). Lackman *et al* (*9*) reviewed 63 patients with grade II or III GCT treated with extended curettage, high concentration (90%) phenol and PMMA. They excluded cases with pathologic or intra-articular fractures. They reported a 6% local recurrence rate, with good functional outcome. Similar with their study we used phenol application at 90% concentration. In order to minimise systemic absorption of phenol, we preferred to paint the walls of the curetted cavity with sponges impregnated with phenol rather than filling the cavity with the phenol solution. Although lower phenol concentrations have a low theoretical risk for systemic side effects, high concentrations provide more effective elimination of microscopic tumour remnants. We did not observe any systemic adverse effects.

Liquid nitrogen is another effective adjuvant which produces bone necrosis by microvascular thrombosis with subsequent ischaemic bone infarction. Lower rates of local recurrence can be

achieved by cryotherapy, however, complications have been reported related to extensive necrosis of the adjacent cartilage and surrounding soft tissues. Malawer *et al* (*14*) reported their experience with cryotherapy by direct application (pouring into the cavity) in the treatment of 102 patients with GCT. Their overall local recurrence was reported as 7.9% ; complications associated with cryosurgery were pathologic fractures in 5.9%, partial skin necrosis in 2.9% and significant joint degeneration in 1.9%.

PMMA used as a filling material is also considered as an adjuvant. Its tumoricidal effects are explained by heat dispersion during polymerisation and direct toxicity by diffusion of the monomer (*12*). However, the usefulness of PMMA as an adjuvant has been questioned recently (*18*). Experimental studies showed that while the temperature markedly rises in the center of the PMMA mass during polymerisation, the temperature elevation in the periphery is insufficient to produce thermal necrosis at the interface with the adjacent bone (*13,21*). It has also been suggested that PMMA may result in extended bone necrosis if it is used in large amounts (more than two packs) (*10*). PMMA as a filling material provides immediate stability allowing early weight bearing and permits early detection of recurrence, more easily than with bone grafting (*2*). There are some concerns regarding the use of PMMA in juxtaarticular locations as it can possibly lead to cartilage degeneration. However experimental and clinical data support its use in subchondral bone (*8,19*). In our study, the bone cement was applied over a thin layer of cancellous bone graft if subchondral bone was exposed by the tumour or during extended curettage, as recommended by Campanacci *et al* (*4*). Only one patient in this series developed radiological signs of osteoarthritis.

Postoperative fracture is an inherent risk due to the presence of a large bone defect or extensive cortical destruction resulting from the tumour or created by the curettage. The risk is higher in patients who are treated with cryosurgery as the latter produces deeper necrosis and delayed regeneration than other adjuvants (*22*). Postoperative fracture rates ranging from 6.9% to 25% after cryosurgery have been reported (*14*). Lewis *et al* (*11*) treated 37 patients with extended curettage and APC. Four of their cases developed postoperative fractures. Of note is the fact that none of the reported cases with fracture had received internal fixation in these studies. Internal fixation was used extensively in our study in weight bearing bones. All but one of our cases with involvement of long bones in the lower extremity received plate or screw augmentation. As a result, reconstruction failed in only one patient who had extensive proximal tibial involvement.

In spite of lower local recurrence rates, the risk of distant metastasis does not decrease with aggressive local management. We observed lung metastases in two cases, neither of which had a local recurrence. In spite of the benign nature of the tumour, lung metastasis may be fatal (*1,17*). Both of our cases were recognised when their lung nodules were small. We strongly recommend close surveillance of patients for at least two years postoperatively.

There are some limitations in this study. First, the mean follow-up (33.7 months) of the patients is relatively short. However, majority of the recurrences occur during the first two years (*20*). Therefore, the duration of the follow-up may be regarded as acceptable. Secondly, the number of subjects in this study was not sufficient to allow for statistical analysis of factors possibly contributing to the rate of local recurrence. Although this retrospective study presents the experience of a single surgeon using a standardised method in the treatment of GCT, the rate of local recurrence (4%) appears as one of the lowest in the literature. We believe that the combined use of effective local adjuvants including high speed burr, argon plasma coagulation and high concentration of phenol resulted in a high rate of eradication of the tumour. The postoperative fractures were avoided by reconstruction of the defect with PMMA and augmented with internal fixation in weight-bearing bones.

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