Aggressive giant cell tumour of bone

Faisham W I, Zulmi W, Halim A S, Biswal B M, Mutum S S, Ezane A M

ABSTRACT

Introduction: The surgical treatment of Stage III or aggressive giant cell tumour of the bone, whether to perform intralesional or en-bloc resection, remains controversial. The aim of this study is to identify the effectiveness of en-bloc resection for local control and final oncological outcome of the disease.

Methods: The data of 20 consecutive patients with Stage III giant cell tumour were retrospectively reviewed to determine the local control and oncological outcome after treatment with wide resection.

Results: The majority of the patients presented late with mean duration of symptoms of 24 months, and four patients presented with recurrences. All patients were treated with wide resection except for two patients who underwent ablative surgery due to major neurovascular involvement. Ten patients required free vascularised tissue transfer to cover massive soft tissue defect. Local recurrence occurred in one patient who was again treated with wide resection and vascularised flap. Six patients had pulmonary metastases. Two patients with resectable disease were treated with thoracoscopic surgery and they remained disease-free 36 months after surgery. Two patients with multiple lung metastases were treated with chemotherapy and the disease remained non-progressive. The remaining two patients who refused chemotherapy showed radiological progression, and one succumbed to the disease with massive haemoptysis.

Conclusion: Aggressive giant cell tumour of bone should be treated with wide resection for better local control, and treatment of pulmonary metastases is mandatory for overall prognosis.

Department of Orthopaedics
Musculoskeletal Oncology Unit
School of Medical Science
Universiti Sains Malaysia
Kubang Kerian 16150
Kelantan
Malaysia

Faisham W I, MMed
Lecturer

Zulmi W, MS
Professor

Plastic Surgery and Reconstructive Unit

Halim A S, FCCP
Associate Professor

Department of Oncology and Radiotherapy

Biswal B M, MD, DNB
Lecturer and Head

Department of Pathology

Mutum S S, MD
Associate Professor

Department of Radiology

Ezane A M, MMed
Lecturer

Correspondence to:
Dr WI Faisham
Tel: (60) 9 766 3000 ext 4511
Fax: (60) 9 765 3370
Email: faisham@kb.usm.my

Keywords: aggressive giant cell tumour, bone tumours, giant cell tumour, wide resection

Singapore Med J 2006; 47(8):679-683

INTRODUCTION

Giant cell tumour (GCT) of bone is a benign but locally aggressive neoplasm, characterised by a large number of uniformly-distributed osteoclast-like giant cells in a bland stroma of spindle-shaped mononuclear cells. Stage III or aggressive giant cell tumour is a symptomatic, rapidly-growing lesion that is often associated with spontaneous fracture. Isotope bone scans show intense activity that often extends beyond the lytic area on radiograph[1,2]. Magnetic resonance (MR) imaging shows infiltration of surrounding soft tissue, confirmed histologically by tumour that has breached the cortex and extended into the surrounding soft tissue.

Treatment of GCT of bone is basically surgical intervention by curettage and adjuvant treatment to eliminate any remnant of tumour, and reconstruction of osseous defect with bone graft or methylmetacrylate[3,4]. However, the treatment of Stage III GCT, i.e. whether to perform an intralesional or en-bloc resection, remains controversial[5,6]. The aim of this study is to identify the effectiveness of en-bloc resection for local control and final oncological outcome of the disease.

METHODS

20 patients with histologically-proven Stage III GCT seen at our institution between January 1997 and June 2003 were included. The clinical and radiological records of all the patients were reviewed. As a part of staging process, routine haematological and biochemical investigations, MR imaging of the primary tumour, whole body bone scintigraphy and computed tomography (CT) of the chest were done. Tissue diagnosis was obtained in all cases with either open or trucut biopsy.

Wide resection, which consisted of removal

Table I. Series of patients with Stage III giant cell tumour of the bone.

Case no.	Sex	Age	Sites	Remarks	Surgical procedures	Lung metastases	Outcomes
1.	M	32	Lt proximal tibia		Fibular composite allograft		Infection
2.	F	24	Lt distal tibia		Fibular composite allograft		SWD
3.	F	23	Rt distal radius		Fibular graft		SWD
4.	F	33	Rt distal femur		Endoprosthesis		SWD
5.	M	20	Rt distal femur	Metachronous distal radius	Above knee amputation	Single nodule – resected	SWD
6.	M	33	Rt distal radius		Fibular graft		SWD
7.	M	63	Lt proximal tibia	Dormant 9 years	Above knee amputation	>5, both lobes	DOD 6 months – massive haemoptysis
8.	F	32	Lt distal femur		Endoprosthesis, free flap		SWD
9.	M	21	Lt distal femur	Recurrent – quadriceps infiltration	Double vascularised fibular graft knee orthrodesis	>5, both lobes	Asymptomatic – progression of nodule
10.	M	41	Lt distal radius		Fibular graft		SWD
11.	F	43	Lt proximal fibula	Recurrent – knee joint infiltration	Endoprosthesis, free flap	Double nodule – resected	SWD
12.	M	28	Rt distal radius	Recurrent	Vascularised fibular graft	>5, both lobes – chemotherapy	Asymptomatic – static
13.	M	35	Lt distal radius		Fibular graft		SWD
14.	M	24	Rt proximal tibia		Endoprosthesis		SWD
15.	M	27	Rt proximal tibia		Endoprosthesis	>5, both lobes – chemotherapy	Asymptomatic – static
16.	M	43	Rt distal femur		Endoprosthesis		SWD
17.	M	28	Rt distal radius		Vascularised fibular graft		SWD
18.	F	33	Rt distal radius	Skin infiltration	Vascularised fibular graft		SWD
19.	F	50	Lt distal ulna	Skin infiltration	Fusion, free tissue transfer		SWD
20.	M	30	Rt distal ulna		Wrist fusion		SWD

SWD: survived without disease; DOD: died of disease; Lt: left; Rt: right

of the tumour en-bloc with a cuff of normal tissue around the mass, was done according to biological anatomical barrier and MR imaging features. The surgical specimens were evaluated for microscopical extent of tumour at the margins and intramedullary marrow extension. Serial CT of the chest and whole body Technetium 99m bone scintiscans were taken at six-monthly intervals for two years and yearly thereafter for five years. Optional local radiological assessments were performed based on symptoms. The outcome of treatment in terms of local control and failure were recorded. Final oncological outcome and presence of pulmonary metastases and major complication in all patients were documented.

RESULTS

There were 13 male and seven female patients, with a mean age of 33 years (range 24-58 years). The location of primary tumours was the distal femur in five patients, proximal tibia in four, distal radius in seven, distal ulna in two, and one each in the proximal fibula and distal tibia. The median follow-up period for all patients was 30 months, ranging from 12 to 60 months. The most common presenting symptom was a painful bony swelling that occurred in 18 (90%) patients. Two patients presented late with arthritic pain and progressive swelling. Four patients presented with recurrent disease after primary treatment. Four patients presented with skin infiltration secondary to previous surgery and biopsy. 16 patients presented late before a definitive diagnosis was made (range six months to nine years), with a mean duration of symptoms of 24 months (Table I).

Classical histopathological features of GCT

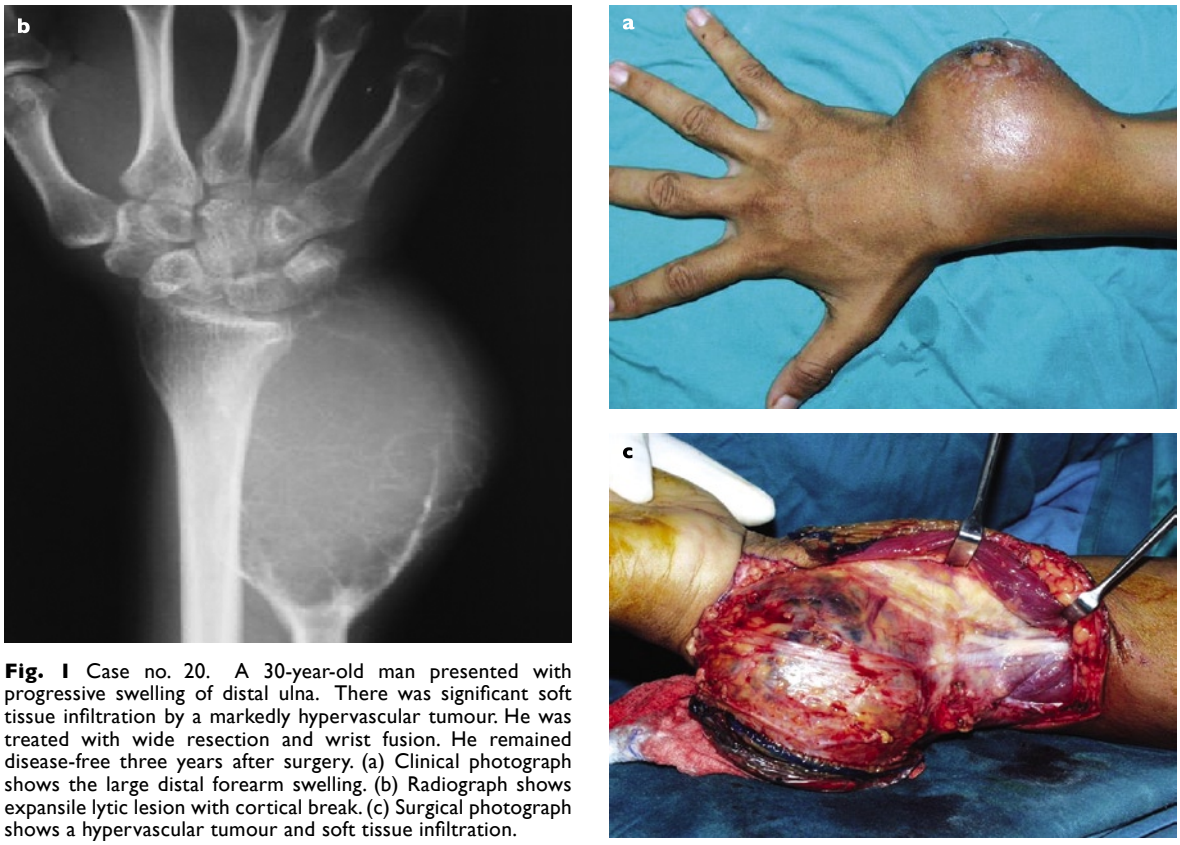

Fig. 1 Case no. 20. A 30-year-old man presented with progressive swelling of distal ulna. There was significant soft tissue infiltration by a markedly hypervascular tumour. He was treated with wide resection and wrist fusion. He remained disease-free three years after surgery. (a) Clinical photograph shows the large distal forearm swelling. (b) Radiograph shows expansile lytic lesion with cortical break. (c) Surgical photograph shows a hypervascular tumour and soft tissue infiltration.

of the bone were observed in all patients. No histological evidence of malignant transformation was seen in any of the cases. Wide margin with 1 cm surrounding normal soft tissue was achieved in 16 cases and marginal of 1-2 mm in another four patients. Four patients with ulcers showed infiltration of the skin and the subcutaneous tissue. Amputation was the primary mode of surgical treatment in two patients. One patient presented with metachronous lesion of distal femur and distal radius. The lesion in distal femur had massive soft tissue infiltration and neurovascular infiltration posteriorly that precluded limb salvage surgery. Another patient presented nine years after initial diagnosis with aggressive behaviour and massive soft tissue and neurovascular involvement.

Limb salvage surgery was performed in 18 patients (Table I). All surgical specimens were evaluated for microscopical extension at the tumour margin and intramedullary marrow extension, and they were tumour-free in all cases. The osseous defects following resection of lower limb were reconstructed with endoprosthesis in seven patients. In one patient with recurrent tumour, the distal femur was reconstructed with double vascularised osteocutaneous fibular graft knee arthrodesis due to massive tumour infiltration into the quadriceps compartment. The proximal tibial osseous defects in two patients were bridged with combined allograft and intramedullary vascularised fibular graft and knee arthrodesis. One patient who had distal tibial lesion was also treated with allograft fibular composite for ankle arthrodesis.

Aggressive lesions in distal radius were treated with a wide resection of margin in all patients. Vascularised osteocutaneous fibular grafts were performed in three patients due to massive soft tissue involvement and skin infiltration. The other three patients were treated with non-vascularised autogenenous ipsilateral fibular graft. Resection of the distal ulnar lesion resulted in wrist instability and massive soft tissue and skin defect. Osseous stability was achieved by wrist arthrodesis and pedicle lateral thigh flap was performed in this case to provide the soft tissue coverage (Fig. 1).

Local recurrence developed 12 months after surgery in one patient with a proximal tibial lesion, which was treated with wide resection and endoprosthesis reconstruction. The recurrent lesion was resected with wide margin, and reconstructed with vascularised latissimus dorsi flap. The patient was disease-free 24 months after surgery. Another patient with distal radius lesion developed a single skin nodule at the dorsal aspect after nine months. It was resected and the patient remained free of the disease.

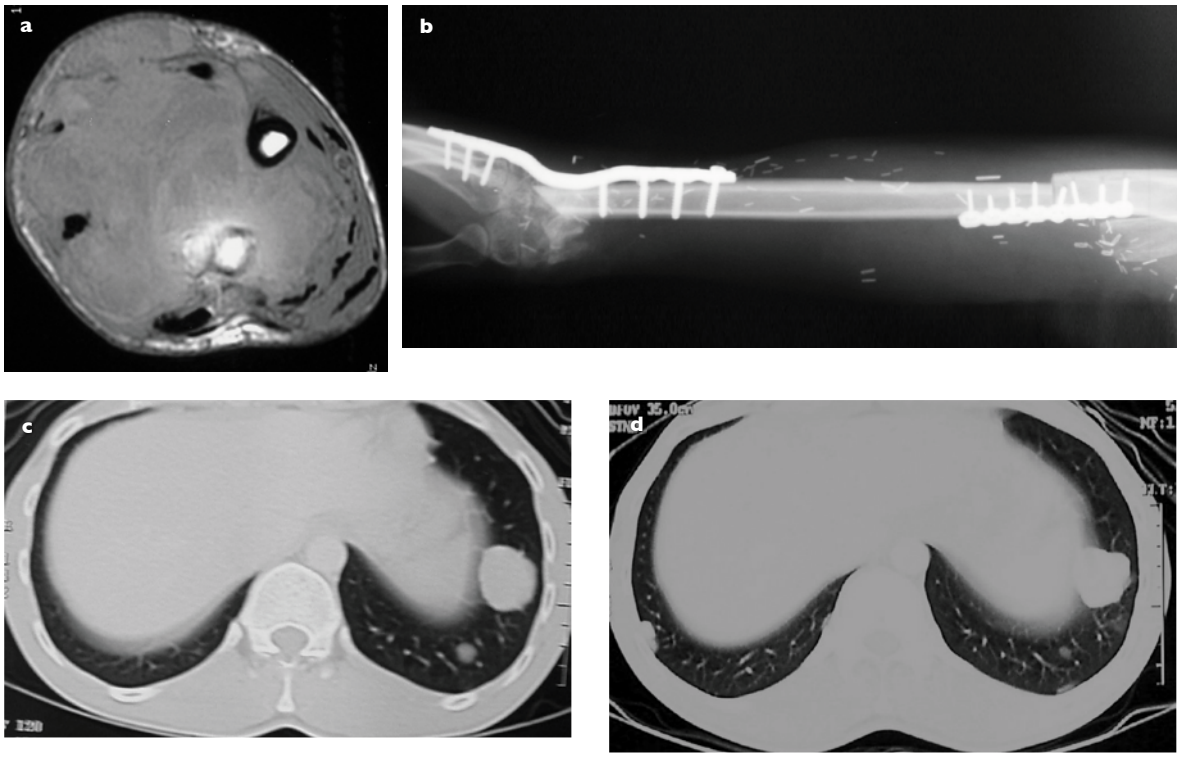

Fig 2. Case no. 12. A 28-year-old man presented with recurrent tumour of the distal radius, which was resected and reconstructed with vascularised fibular graft. He also had multiple pulmonary metastases that precluded surgical resection. He received six courses of adriamycin and cisplatin for six months. At present, he is asymptomatic and pulmonary nodules remain static. (a) Axial T1-W MR image shows distal radius giant cell tumour with massive soft tissue involvement. (b) Postoperative radiograph shows the vascularised fibular graft and wrist fusion. Axial CT images (c) at presentation shows multiple pulmonary metastases, and (d) after three years, shows no progression of pulmonary nodules.

Six patients had pulmonary metastases, and four presented with recurrence of lesion after intralesional surgery. One patient presented after nine years with locally-aggressive lesion and another patient had metachronous tumour of distal femur and radius. Two patients who had single and double metastatic tumour nodules, respectively, in the lung underwent thoracoscopical resection. Both were disease-free at 36 months after surgery. Two patients who had multiple nodules in the lung received six courses of adriamycin and ifosfamide. They remained asymptomatic and showed resolution with peripheral calcification of pulmonary nodules (Fig. 2).

The two patients who refused chemotherapy showed progression of the lung nodules. One patient subsequently succumbed to the disease at six months with massive haemoptysis. Two patients treated with fibular composite allograft developed chronic infection, which was controlled with repeated debridement and antibiotics. Both patients achieved osseous union 12 months after surgery, despite developing infections.

DISCUSSION

GCT is an infrequent and unpredictable bony lesion[7]. Although numerous attempts have been made to predict the behaviour of GCT, there are no definite biological or histological parameters to determine the prognosis or aggressiveness of this lesion[8]. A review of the histopathological evaluations in the patients in this series did not reveal any evidence of malignant change, despite being locally aggressive. The aggressive behaviour of GCT seems to occur more frequently in the oriental population[9,10]. In our patients, GCT not only presented with locally-aggressive behaviour, it also had higher incidence of pulmonary metastases.

The treatment for GCT of bone is basically surgical resection. The decision whether to perform an intralesional excision (curettage) or en-bloc resection of the tumour, is based on local tumour extension[3-5,11]. Curettage has been associated with a high rate of local recurrence that ranges from 22% to 40%[3-5]. Combination with adjuvant treatment, such as the use of phenol and methylmethacrylate, reduces the incidence of recurrence to less than 10%[3,4]. The local recurrence has been shown to correlate with aggressiveness of the lesion.

A sequential increase in local recurrence rate from Stage I to III with 7% in "quiescent", 26% in "active", and 41% in "aggressive" tumours respectively, has been observed[4]. The patients with multiple local recurrences are more likely to develop metastases[4]. In our series, the patients had either presented late or had recurrent lesions with surrounding soft tissue infiltration. Wide resection has been shown to be a good alternative for local control of stage III disease with 5% recurrence[5,6].

Amputation may be a good option for GCT of

bone that has an aggressive behaviour, particularly with massive skin infiltration. However, the local aggressive behaviour has not been shown to change the final outcome and prognosis of the patients[4]. This has to be considered in the final treatment. All patients with skin infiltration in this series had good local control after wide removal of the skin together with the tumour and reconstruction with vascularised flap.

Biological reconstruction of the osseous defect should be considered first. This is pertinent as the disease occurs in younger patients, whose functional demands are high and who have higher life expectancies[11]. Osteomyocutaneous vascularised fibular graft is, in our opinion, the best option to reconstruct the distal radius and provides good cover over the soft tissue defect. A combination of allograft constructs with vascularised fibular graft as in a knee arthrodesis provides early stability and reduces the long-term complication of allograft. This is also shown by others investigators[12,13]. It enhances healing and provides almost total biological incorporation in long-term follow-up. Biological reconstruction with vascularised fibula osteocutaneous graft or combination of allograft fibular flap composites is a good alternative construct for reconstruction of both osseous and soft tissue defects with better long-term results as shown in our series.

Endoprosthetic reconstructions provide immediate stability and allows early mobilisation and weight-bearing. The advancement and modularity of present implant have dramatically improved function with better long-term outcome. It is too early to predict the outcome of endoprosthesis in our series. However, in other series, ten- to 15-year survival with endoprosthesis have been reported in about 70-75%, despite the young age of the patients in whom the prosthesis was implanted[14].

Approximately 1-2% of GCT of bone develop metastases that are histologically identical to the primary tumour[3,4,15-18]. Surgical staging, based on combination of clinical, radiographical and pathological findings, has shown that aggressive lesions and recurrences are found to be main risk factors for pulmonary metastases[4]. Local recurrence is associated with 6% incidence of metastatic disease, and in patients without local recurrence, this incidence is less than 1%[4]. The incidence of pulmonary metastases was higher (30%) in our series. This raises a question mark about the actual behaviour of GCT in the oriental population.

The natural history of metastatic pulmonary disease has been found to be as unpredictable as the primary tumour[4,7]. Solitary and surgically-accessible lesions can be resected with excellent long-term survival[6,15]. Multiple and asymptomatic lesions may remain stationary in size, or even spontaneously regress without therapy. In symptomatic and unresectable pulmonary metastases, radiotherapy has been reported with variable results and with the risk of secondary sarcomatous transformation[6,15]. Chemotherapy in combination with surgery also has a significant value to control the disease and symptoms in selected patients[16]. The patients with multiple pulmonary metastases in our series did benefit with six courses of chemotherapy. They were asymptomatic for 24 months, and serial CT showed a peripheral rim of calcification and no progression of the lesion.

In conclusion, Stage III GCT of bone is best managed with wide resection for better local control. Aggressive treatment of pulmonary metastasis is mandatory in the management of aggressive GCT. The prognosis is favourable in patients with complete surgical resection of pulmonary nodule or those who have received chemotherapy. The overall outcome of treatment is good.

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