F. Malek · P. Krueger · Z. N. Hatmi · A. A. Malayeri ·
H. Faezipour · R. J. O'Donnell

Local control of long bone giant cell tumour using curettage, burring and bone grafting without adjuvant therapy

Received: 13 December 2005 / Revised: 20 February 2006 / Accepted: 28 February 2006 / Published online: 2 August 2006
© Springer-Verlag 2006

Abstract Giant cell tumour (GCT) is a benign, but aggressive, primary tumour of the bone. The recurrence rate after surgical treatment has been reported to be as high as 50%. Many surgical techniques have been employed in the treatment of this tumour. More aggressive interventions, such as en bloc resection and bulk allograft or prosthetic reconstruction, are generally understood to be associated with lower rates of local recurrence. However, because of lessened morbidity, intralesional techniques have come to be favoured for this condition. In addition to curettage, various adjuvant procedures and packing materials have been advocated in order to control and reconstruct long bone defects secondary to this neoplasm. We report our experience with 40 long bone GCT patients treated with curettage, burring, bone grafting and no adjuvants between 1997 and 2002. There was a local recurrence rate of 32.5%, with most recurrences noted within the first 30 months after surgery. Minor complications were found in 18% of patients. The risk of local recurrence in this study is acceptable (within the range that has been historically reported for curettage and bone grafting). In cases where more resources are available, the addition of adjuvant therapies, as noted in the recent literature, may be beneficial. The results of this study should be considered when designing multicenteric studies in the future.

Résumé Les tumeurs à cellules géantes sont bénignes et agressives localement. Le taux de récurrence après traitement chirurgical est important (50%). Beaucoup de techniques chirurgicales ont été utilisées dans le traitement de ces tumeurs. Des techniques très agressives comme la résection en bloc et une allogreffe massive ou une reconstruction prothétique ont pu être proposées avec un taux de récurrence faible. Cependant du fait d'une morbidité moindre des techniques de traitement local de la tumeur ont pu être utilisées dans des conditions favorables. Après curetage, différentes procédures de reconstruction ont été réalisées. Nous rapportons notre expérience de 40 tumeurs à cellules géantes traitées par curetage, bourrage, greffes sans adjuvant particulier entre 1997 et 2002. Le taux de récurrence a été de 32,5%, surtout dans les 30 premiers mois. Après l'intervention chirurgicale des complications mineures ont été retrouvées dans 18% des cas. Le risque de récurrence locale, dans cette étude est acceptable.

Introduction

GCT comprises approximately 10% of primary musculoskeletal tumours [6]. There is a slight predilection for women, with an average age of 30 years. The most common long bone locations are the distal femur, proximal tibia, distal radius, proximal femur, and proximal humerus. The radiological appearance is that of a geographic, lucent, eccentric, and meta-epiphyseal lesion, extending to subchondral bone, sometimes with soft tissue extension [6]. Multicentricity, pulmonary metastasis, and malignant transformation have all been reported [17, 22].

Various surgical methods have been proposed for treatment of giant cell tumour, but there is no established protocol, and controversies still exist. When formulating a plan for local control of a long bone GCT lesion, the surgeon must decide whether to perform an en bloc resection or an intralesional procedure, whether to add adjuvant therapy in order to attempt to eradicate microscopic residues, and whether to use any of a variety of packing materials for the defect. Local recurrence rates

F. Malek (✉) · P. Krueger · R. J. O'Donnell
San Francisco Department of Orthopaedic Surgery UCSF
Comprehensive Cancer Center Orthopaedic Oncology Service,
University of California,
1600 Divisadero Street,
San Francisco, CA 94115-1939, USA
e-mail: farbodmalek@yahoo.com
Tel.: +1-415-8853800
Fax: +1-415-8853802

F. Malek · Z. N. Hatmi · A. A. Malayeri · H. Faezipour
Cancer Institute, Orthopaedic Oncology Service,
Tehran University of Medical Sciences,
Tehran, Iran

after resection and bulk allograft reconstruction have been reported to be as low as 0 percent [5, 9]. Reported local recurrence rates after intralesional procedures have ranged from 0 to 52 percent [1, 2, 4, 5, 8, 9, 13, 15, 18–21, 25]. Factors associated with obtaining local control have included the use of a burr [2], phenol [5, 16, 22], electrocautery [25], cryosurgery [22], hydrogen peroxide [25], autograft bone [2, 19–21], allograft bone [2, 19–21], and polymethylmethacrylate bone cement (PMMA) [1, 4, 16, 20]. Recently, very acceptable rates of local control have been reported using curettage alone, without adjuvant therapies or packing [18]. This approach is especially appealing in developing areas of the world, where resources, in terms of radiographic imaging, surgical instruments and supplies, and clinical surveillance capability, may be somewhat limited. We report a single institutional experience from the Cancer Institute, Tehran, Iran, with 40 long bone GCT patients treated with curettage, burring, bone grafting, and no adjuvant measures.

Materials and methods

A retrospective descriptive cohort study was undertaken to identify all patients presenting with a primary giant cell tumour involving a long bone at the Meraj Clinic of the Cancer Institute of Imam Hospital in Tehran, Iran, between 1997 and 2002. Office records, operative notes, hospital charts, and radiographs were reviewed for pertinent data, including gender, age, tumour location, grade [3], presence of pathological fracture, surgical technique, length of postoperative follow-up, and evidence of local recurrence. An intralesional surgical technique was used similar to that described previously [13]. After the creation of a cortical window of sufficient size to visualise the entire tumour cavity, neoplastic tissue was removed with

aggressive manual curettage followed by extension of the margins using a high-speed power burr. The cavity was then irrigated with sterile water, without the use of adjuvants. The subchondral area was packed with autogenous iliac crest cancellous bone, and the remainder of the cavity was filled with allograft cancellous bone. Patients lost to follow-up earlier than 18 months after surgery were excluded from the study with respect to local recurrence rates. The Kaplan-Meier method was used to determine tumour-free survival [12]. A 95% confidence interval was calculated by the Greenwood method [11].

Results

Forty-seven patients were identified with histological confirmation of the diagnosis of long bone giant cell tumour. Seven patients were lost to follow-up. Of the remaining 40 patients, the average follow-up time was 48 months (range 18–78). There were 21 women and 19 men, with an average age of 43.5 years (range 12–75). Tumour location included distal femur (13), proximal tibia (9), proximal fibula (5) proximal humerus (2), distal tibia (4), distal humerus (1), distal radius (1), proximal femur (1), and others (4). Pathological fracture occurred at presentation in 7 of 40 patients (17.5%). There were 2 patients (5%) presenting with grade 1 tumours, 26 patients (65%) with grade 2, and 12 patients (30%) with grade 3. Thirteen of the patients (32.5%) had local recurrence. According to the Kaplan-Meier survival plot with a 95% confidence interval, the 30-month tumour-free survival was 78 percent (Fig. 1).

The mean length of time to recurrence was 28 months (range 9–60). Neither gender, age, anatomical location, presence of pathological fracture, nor Campanacci grading were predictive of local recurrence in a statistically significant manner.

Fig. 1 Kaplan-Meier plot with 95% confidence interval shows 78 percent tumour-free survival within the 30 months after surgery

All 40 patients had a functional limb after operation. All patients with lower limb lesions were able to walk after 6 to 8 weeks rehabilitation.

Seven patients had postoperative complications. These complications included two non-unions, three cases of decreased range of motion, and two patients with superficial wound infections.

Discussion

Long recognised as a benign, but potentially aggressive neoplasm, GCT has historically been approached in a suitably aggressive manner. With the advent of bulk cortico-cancellous and massive osteoarticular allografts, and, later, with the increased availability of endoprosthetic devices, en bloc resection often come to replace intralesional procedures for local control of long bone GCT. Although there are few reported series, local recurrence rates after such wide resections have been, predictably, quite low. For example, Gitelis et al. [9] reported no local recurrences after the treatment of 20 long bone GCT patients with en bloc resection after a mean follow-up of 92 months. Most recently, Mankin and Hornicek [14] reported a local recurrence rate of 6% in such cases. Nonetheless, allograft usage is associated with high rates of infection, fracture, and non-union, with approximately one third of patients suffering at least one major complication [14, 15]. Similarly, massive prosthetic implants are also subject to complications such as aseptic loosening and deep infection, often necessitating revision, and sometimes even amputation [24].

Because of the relatively high rate of major complications and the adverse functional effects of en bloc resection, intralesional treatment of long bone GCT gained renewed interest after the widespread introduction of PMMA packing for this clinical situation in 1969, by Vidal et al. [23]. For example, O'Donnell et al. reported a 25% local recurrence rate after the treatment of 60 GCT patients with curettage and packing with PMMA. However, acceptable rates of local control are still reported with allograft or autograft packing [2, 19–21], or even no packing [18]. In a recent study, Prosser et al. [18] retrospectively reviewed 137 GCT patients treated primarily with curettage without adjuvant therapy over a 27-year period. They reported an overall 19% local recurrence rate. The benefits of decreased morbidity and improved function associated with intralesional procedures have been, in general, thought to outweigh the disadvantage of a higher local recurrence and re-operation rate than was traditionally associated with en bloc procedures. Nonetheless, a caveat for complete reliance on intralesional procedures has been reported, insofar as both O'Donnell et al. [16] and Prosser et al. [18] noted local recurrence rates of 37.5 and 29%, respectively, for tumours with extraosseous extension (grade 3).

In order to further decrease the rates of local recurrence, a variety of adjuvant measures have been employed and reviewed for effectiveness. These additive steps include

mechanical burring, electrocautery, and/or the application of a variety of substances, including hydrogen peroxide, phenol, and liquid nitrogen. For example, Ward et al. [25] reported a 6.4% rate of local recurrence after intralesional resection of GCT consisting of curettage, burring, hydrogen peroxide application, electrocautery, phenol irrigation, and reconstruction with PMMA. To date, no prospective, randomised controlled study exists to document the efficacy of any one adjuvant measure or a combination of measures.

In developing countries, where provision of clinical care is limited not only by health care resources, but by the ability of patients to present for care in a timely fashion and to attend follow up appropriately, there is interest in treatments that are not only effective, but also reproducible in community settings where access to care may be impaired. To this end, we undertook the current study to evaluate our efforts to establish local control of long bone GCT without en bloc techniques, bone cement packing, or any adjuvant measures.

The demographic characteristics of our patients with respect to age, sex, and anatomical location were similar to those of previous studies. There was a female predominance, with most patients between 20–40 years of age, and 67.5% of tumours were located about the knee [6, 7, 9]. However, although we found no direct correlation between Campanacci grade and local recurrence, our small cohort did present with a higher percentage of grade 3 tumours (30%) than is commonly found in the literature [1, 9], suggesting a delay in presentation in our patient population. There is some evidence that late or delayed presentation in this fashion may be associated with higher recurrence rates [16, 18].

Recurrences in patients treated for long bone GCT are common and most often occur within the first two years postoperatively [2, 4, 6]. The local recurrence rate of 32.5% noted in our study is within the range reported in the literature for curettage and bone grafting, which ranges from 12 [2] to 52% [10]. Considering these historical controls, and the limitations of our population in terms of access to care, our reported recurrence rate is understandable and can be readily reduced further, as has been reported following the use of adjuvant therapies.

Our study can serve as the basis for the development of more global or at least national guidelines for the management of this condition. That is to say, by establishing acceptable local control rates using techniques that are thorough and meticulous yet cost effective, readily available, and applicable to smaller centers, it is hoped that the standard of care level can be raised for the entire populace. It is thus recognized that obtaining medical education aimed at improving the quality of surgical techniques is important. However, socio-economic factors that can be altered to favourably influence delay in diagnosis and access to follow-up care may be equally important. To this end, prospective controlled studies will be helpful in order to eliminate such socio-economic variables when attempting to study the effects on outcome that different local control techniques might have.

References

1. Bini SA, Gill K, Johnston JO (1995) Giant cell tumour of bone. Curettage and cement reconstruction. *Clin Orthop Relat Res* (321):245–250
2. Blackley HR, Wunder JS, Davis AM, White LM, Kandel R, Bell RS (1999) Treatment of giant-cell tumours of long bones with curettage and bone-grafting. *J Bone Joint Surg Am* 81 (6):811–820
3. Campanacci M (1976) Giant-cell tumour and chondrosarcomas: grading, treatment and results (studies of 209 and 131 cases). *Recent Results Cancer Res* (54):257–261
4. Campanacci M, Baldini N, Boriani S, Sudanese A (1987) Giant-cell tumour of bone. *J Bone Joint Surg Am* 69(1):106–114
5. Capanna R, Fabbri N, Bettelli G (1990) Curettage of giant cell tumour of bone. The effect of surgical technique and adjuvants on local recurrence rate. *Chir Organi Mov* 75(1 Suppl):206
6. Dorfman HD, Czerniak B (1998) Bone tumours. In: Dorfman HD, BC (eds) *St.Louis, Mosby*, pp 559–606
7. Enneking WF (1986) A system of staging musculoskeletal neoplasms. *Clin Orthop Relat Res* (204):9–24
8. Ghert MA, Rizzo M, Harrelson JM, Scully SP (2002) Giant-cell tumour of the appendicular skeleton. *Clin Orthop Relat Res* (400):201–210
9. Gitelis S, Mallin BA, Piasecki P, Turner F (1993) Intralesional excision compared with en bloc resection for giant-cell tumours of bone. *J Bone Joint Surg Am* 75(11):1648–1655
10. Goldenberg RR, Campbell CJ, Bonfiglio M (1970) Giant-cell tumour of bone. An analysis of two hundred and eighteen cases. *J Bone Joint Surg Am* 52(4):619–664
11. Kalbfleisch JD, Prentice RL (1980) In: *The Statistical analysis of failure time data*. New York, Wiley
12. Kaplan EL, Meier P (1958) Nonparametric estimation from incomplete observation. *Journal of American Statistical Association* 53:457–481
13. Lin PP, J FS (2005) Intralesional treatment of bone tumours. *Operative Techniques in Orthopaedics* 14:251–258
14. Mankin HJ, Hornicek FJ (2005) Treatment of giant cell tumours with allograft transplants: A 30-year study. *Clinical Orthop Relat Res* (439):144–150
15. Masui F, Ushigome S, Fujii K (1998) Giant cell tumour of bone: a clinicopathologic study of prognostic factors. *Pathol Int* 48(9):723–729
16. O'Donnell RJ, Springfield DS, Motwani HK, Ready JE, Gebhardt MC, Mankin HJ (1994) Recurrence of giant-cell tumours of the long bones after curettage and packing with cement. *J Bone Joint Surg Am* 76(12):1827–1833
17. Peimer CA, Schiller AL, Mankin HJ, Smith RJ (1980) Multicentric giant-cell tumour of bone. *J Bone Joint Surg Am* 62(4):652–656
18. Prosser GH, Baloch KG, Tillman RM, Carter SR, Grimer RJ (2005) Does curettage without adjuvant therapy provide low recurrence rates in giant-cell tumours of bone? *Clin Orthop Relat Res* (435):211–218
19. Richardson MJ, Dickinson IC (1998) Giant cell tumour of bone. *Bull Hosp Jt Dis* 57(1):6–10
20. Saglik Y, Yildiz Y, Karakas A, Ogut H, Ereku S (1999) Giant cell tumour of bone. *Bull Hosp Jt Dis* 58(2):98–104
21. Sung HW, Kuo DP, Shu WP, Chai YB, Liu CC, Li SM (1982) Giant-cell tumour of bone: analysis of two hundred and eight cases in Chinese patients. *J Bone Joint Surg Am* 64(5):755–761
22. Truncate RE, Wunder JS, Isler MH, Bell RS, Schachar N, Masri BA, Moreau G, Davis AM (2002) Giant cell tumour of long bone: a Canadian Sarcoma Group study. *Clin Orthop Relat Res* (397):248–258
23. Vidal J, Mimran R, Allieu Y, Jamme M, Goalard G (1969) *Plastie de Complement par Metacrylate de Methyle Traitment de Certaines Tumeurs Osseuses Benignes*. Montpellier Chir 15:389–397
24. Ward WG Sr, Dory F, Kelly C, Kabo JM, Wirganowicz PZ, Eckardt JJ (1999) Lessons from massive tumour endoprostheses: Implications for future tumour and total joint endoprostheses. *Seminars in Arthroplasty* 10(3):124–132
25. Ward WG Sr, Li G 3rd (2002) Customized treatment algorithm for giant cell tumour of bone: report of a series. *Clin Orthop Relat Res* (397):259–270