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Giant cell tumors of bone: nonsurgical factors associated with local recurrence

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Objective: To determine the rate of giant cell tumor (GCT) recurrence and evaluate the factors associated with its recurrence in patients who underwent surgery and submitted to only one adjuvant method.

Methods: Forty–one patients (22 female, 19 male; mean age: 34.22±9.70 years) with GCT, who underwent surgical and one adjuvant treatment, were evaluated after a mean follow-up period of 40.17±22.08 months. The average tumor size was 8.51 ± 3.69 cm. The tumors in 18 patients (43.9%) were grade II and in 23 patients (56.1%) grade III, according to the system developed by Campanacci et al. The surgical margin was intralesional resection and curettage in 60.9% of the patients, and marginal or wide resection in 39.1%.

Results: Nine (22%) of the 41 patients had recurrence. None of the gender (p=0.436), age (p=0.310), site of the tumor (p=0.940), surgical margins (p=0.400) and the type of the filling material (PMMA or autograft) (p=0.680) had an association with recurrence. However, Campanacci grade III (p=0.028) and the size of the tumor (p=0.034) was associated with the recurrence.

Conclusion: Tumor size and tumor grade III according to the Campanacci system appear to be risk factors for local recurrence after the local resection of GCT.

Key words: Giant cell tumor; neoplasm; prognosis.

Giant cell tumor (GCT) is a primary bone tumor first described in 1918, and then better defined as a specific entity in 1940 by Jaffe.[1] In spite of being benign, GCT is an aggressive lesion that may result in distant metastasis.[2] GCT represents 5% of all bone tumors and 20% of benign tumors; nearly 70% of cases occur between the third and fourth decades of life.[3]

The ideal treatment for these lesions remains controversial. Several procedures are described, from intralesional curettage with or without adjuvant methods (phenol, cryotherapy and ethanol) to wide resections with biological or nonbiological reconstruction (arthroplasty).[4] More aggressive procedures reduce recurrence but increase morbidity and deteriorate functional results. Curettage combined with adjuvant methods preserves adjacent joints and enhances better functional results,

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but it causes a higher risk of recurrence.[4]

Local recurrence varies from 0% to 47% (Table 1).[4-15] This wide range of incidence depends on several factors. Most studies attribute the main role in determining the local control to the surgical technique and adjuvant method. However, there are other factors that may influence recurrence, such as tumor site, size and aggressiveness.

The aim of this study was to determine the rate of GCT recurrence and evaluate the factors associated with the recurrence.

Patients and methods

The study included 41 patients (19 male and 22 female; a mean age: 34.2 years [range, 19–52]) with GCT in the limbs, pelvic and scapular girdle, who underwent surgical treatment in our institution between June 2000 and March 2009. The inclusion criteria were a minimum follow-up of 12 months, and the completeness of the medical records.

Each patient gave full informed consent before entry into the study. Local ethical committee approval was obtained before commencement of the study.

The mean follow–up time was 40.2 months (range, 12–112). All tumors were classified with radiographic images, MRI, radionuclide scan and thorax CT.

The mean size of the tumors was 8.51±3.69 cm (range, 3.0–17.0 cm). The tumor was located in the lower limbs in 28 (68.3%) patients, in the pelvis in 4 (9.8%) and in the upper limbs in 9 (22%). The most common region of involvement was around the knee, with 15 cases (36.5%) (Table 1). According to Campanacci staging system[16]; 18 cases (43.9%) were grade II and 23 (56.1%) grade III.

We performed an intralesional resection in 25 (60.9%) patients (Figure 1). In this method the tumor was curetted through a wide cortical window. Then lavage with saline solution was followed by electrocauterization that continued for at least five minutes, until all the inside surface was darkened due to carbonization debris (Table 1). Finally, a new saline solution lavage was carried out, and the cavity was filled with autograft in 7 (28%) patients or polymethylmethacrylate (PMMA) in 18 (72%) patients.

Wide or marginal resection was performed in 16 (39%) patients. The indications were articular involvement, invasive tumors that would not allow reconstruction after curettage; and some specific sites where segmental resection presents better results, such as distal radius. Of these 16 patients, six (14.6%) underwent reconstruction with arthroplasty, six (14.6%) underwent arthrodesis and four (9.8%) underwent segmental resection with no reconstruction (two in iliac bone and two in the proximal region of the fibula).

Complications were observed in four (9.8%) patients: fractures in two (4.9%), deep infection in one (2.4%), and arthrofibrosis that required manipulation under anesthesia in one (2.4%).

All patients were followed up weekly until complete wound healing, and then monthly until 6th months after surgery. Clinical examination and X-Ray and CT scan were performed every 3 months and chest radiography was performed annually. In recurrent cases surgical treatment was planned after staging.

Statistical analysis: The overall recurrence was evaluated through analysis of the survival curve using the Kaplan–Meier method.

Table 1. Local recurrence rate after two different methods of adjuvant treatment.

Author	Year	Patients (n)	Adjuvant	Recurrence (%)
Saiz et al.[4]	2004	40	Electrocauterization + Phenol	12.5
Capanna et al.[5]	1990	280	None	45
Saglick et al.[6]	1999	21	None	33
O'Donnell et al.[7]	1994	49	Polymethylmethacrylate	24
Turcotte et al.[8]	2002	62	Polymethylmethacrylate	19
Capanna et al.[5]	1990	147	Phenol	19
Su et al.[9]	2004	56	Phenol	18
Malawer et al.[10]	1999	86	Criotherapy	3
Turcotte et al.[8]	2002	10	Criotherapy	0
Zhen et al.[11]	2004	92	Zinc chloridrate	13
Ghert et al.[12]	2002	47	Phenol + Polymethylmethacrylate	13
Ward and Li[13]	2002	24	H_2O_2 + Phenol + Electrocauterization	8
Jones et al.[14]	2007	31	Ethanol	16
Masui et al.[15]	1998	17	None	47

Initially, in order to explore each independent variable in the data set separately, the results were evaluated using a univariate analysis between the variable in question (recurrence) and each of the independent variables. The independent variables were age (≤30 years or >30 years), gender, tumor localization (upper or lower limbs), staging (Campanacci II or III), tumor size, margins (intralesional *vs*. marginal or wide), and in the cases of intralesional resection, the material used to fill the cavity (PMMA or allograft). The univariate analysis was evaluated with the Log Rank test, and the variables that presented p≤0.25 were included in a multivariate analysis by the Cox regression. Results with a p value less than 0.05 were considered statistically significant.

Taking into consideration the segmental nature of the tumor size, the model was adjusted for survival curves, based on the mean and standard deviation (S.D.), into small (μ-s=4.82); medium (μ=8.51) and large (μ+s=12.21).

The statistical analysis was performed using SPSS® 13.0 (Chicago, USA) software.

Results

Nine (22%) patients had recurrence during the follow–up period, which had a mean duration of 13.0±13.5 month (range, 4–47 month). Figure 2 shows the Kaplan-Meier's survival curve for local recurrence expectation. From the postoperative period until the fourth month, the chance of recurrence was 3.4%, between 4 and 12 months after surgery, the chance was 17.1% and after one year of surgical treatment, the chance of recurrence was 20%.

The variables gender (p=0.436), age (p=0.310), site of involvement (p=0.940), surgical resection margins (p=0.400) and the kind of material used to fill the cavity (PMMA or autograft) (p=0.680) had no signicant association with the recurrence.

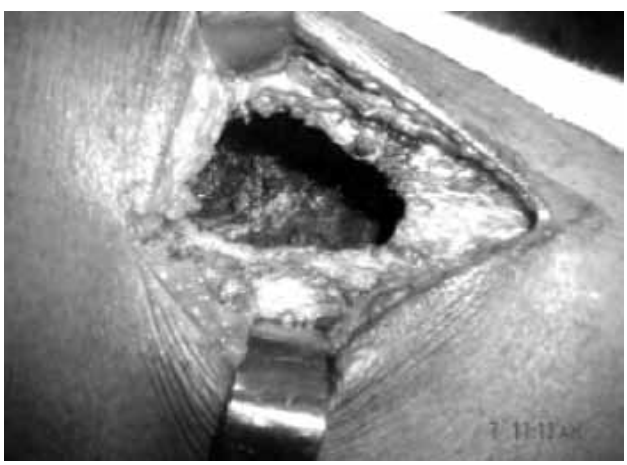

Fig. 1. Clinical photograph after curettage and electrocauterization.

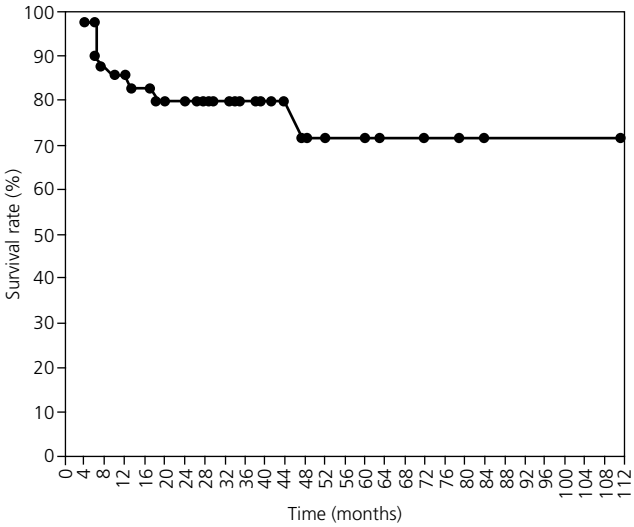

Fig. 2. Kaplan-Meier's survival curve for local recurrence expectation.

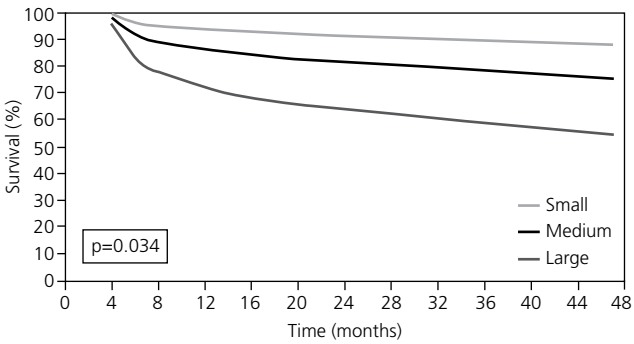

Fig. 3. Survival rate without recurrence according size of tumor.

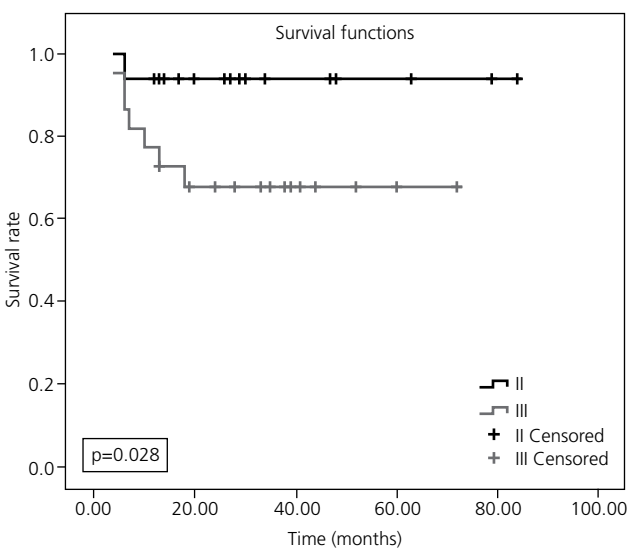

Fig. 4. Survival rate of relapse acording Campanacci et al. staging.[16]

The survival curves showed that "large" tumors had a significantly higher risk of recurrence (p=0.034) (Figure 3). We observed one (5.8%) case of recurrence in 18 tumors of Campanacci grade II, and eight (36.3%) recurrences in 23 tumors of Campanacci grade III. Multivariate analysis confirmed that the stage had a significant association with the recurrence (p=0.028) (Figure 4).

The Cox regression showed that both intralesional and wide resection groups were homogeneous in terms of localization, grading and size.

Discussion

The diversity of results following resection of the GCT depends on several factors. Most studies highlight the surgical technique and adjuvant methods as the main factors for local control of the tumor. However, we believe that other factors should also be considered as a risk for recurrence.

Our study was designed to determine the rate of recurrence of GCT, and evaluate factors other than surgical margins and adjuvant methods associated with recurrence.

In this group, we noticed that size and Campanacci classification were significantly associated with recurrence. The present study agrees with Prosser et al,[2] who considered the completeness of the resection as the most important factor for the success of treatment, but also observed that recurrence was higher in Campanacci grade III (28.8%) than in Campanacci grades I (7.7%) and II (6.8%). However, in disagreement with our study, they did not show the influence of the tumor's size on the recurrence rate. Saiz et al[4] evaluated the recurrence rate in 40 patients who were treated with intralesional resection followed by curettage and cavity filling with PMMA. The recurrence rate was 12.5%; most occurred within one year of follow-up and the longest period for the last recurrence to occur was 38 months. They did not observe differences concerning the following variables: staging, age, gender, complications and tumor location. Jones et al,[14] using ethanol as adjuvant treatment for GCT, in disagreement with our study, did not correlate Campanacci staging with recurrence.

Turcotte et al.[8] in their series of 186 cases of GTC with a mean follow-up of 50 months reported a recurrence rate of 17%. This is a smaller rate than the majority of studies, for which the mean value is 33%. The authors demonstrated that the only variable that increased the rate of local recurrence was the wideness of the resection, and the size and staging were not found to affect the recurrence rate.

In our study, all of the patients with local relapse had observed the event within four years. After this period, the probability of recurrence became steady, as observed by Turcotte et al.[8]

The wideness of the resection was not associated with the recurrence rate in our study. This may suggest that a more wide and aggressive resection was performed for the larger and more aggressive tumors.

The main limitation of our study was its retrospective design.

In conclusion larger tumor size and a Campanacci classification of grade III were associated with local recurrence.

Conflicts of Interest: No conflicts declared.

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