



# Treatment of Patients Diagnosed with Giant Cell Tumor of Bone: Experience of a Philanthropic Hospital in the State of Piauí, Brazil\*

## *Tratamento de pacientes com diagnóstico de tumor ósseo de células gigantes: Experiência de um hospital filantrópico no Piauí, Brasil*

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### Abstract

**Objective** To evaluate the treatment of patients with giant cell tumors of bone treated from 2009 to 2019 in a philanthropic hospital, as well as to try and determine the regional clinical and epidemiological profile, aiming to enrich the Brazilian data set and compare our findings with those of the literature.

**Methods** An analytical, observational, and cross-sectional study with retrospective data collection and a quantitative approach, analyzing medical records of patients with giant cell tumors treated at a philanthropic hospital from 2009 to 2019.

**Results** We evaluated 49 medical records; 55.1% of the patients were women, 53.1% were aged between 20 and 40 years, 69.4% of the cases were Campanacci grade III, and 30.6% affected the proximal end of the tibia. The rate of pathological fractures secondary to the tumor and pulmonary metastasis was low. More than 69% of the patients underwent intralesional surgery. Recurrence occurred in 16.3% of the cases.

**Conclusion** The criteria used for the diagnosis, classification, and treatment at our service followed the standards established by the literature, and they can guide further research and improve local prognosis in the future.

### Keywords

- ▶ giant cell tumors/diagnosis
- ▶ giant cell tumors/classification
- ▶ bone neoplasms

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## Resumo

**Objetivo** Avaliar o tratamento fornecido a pacientes com diagnóstico de tumor de células gigantes ósseo atendidos no período de 2009 a 2019 em um hospital filantrópico, bem como determinar o perfil clínico e epidemiológico regional, visando enriquecer os dados nacionais e comparar os achados com a literatura existente.

**Métodos** Estudo analítico, observacional e transversal, com coleta retrospectiva e abordagem quantitativa, com análise de prontuários de pacientes diagnosticados com tumor de células gigantes atendidos em um hospital filantrópico no período de 2009 a 2019.

**Resultados** Foram avaliados 49 prontuários, sendo que 55,1% eram de mulheres, com 53,1% dos casos na faixa etária de 20 a 40 anos, 69,4% de casos de grau III de Campanacci, e 30,6% acometendo a extremidade proximal da tíbia. Observou-se baixo índice de fratura patológica secundária ao tumor e de metástase pulmonar. A cirurgia intralesional foi realizada em 69,5% dos pacientes. Houve recidiva em 16,3% dos casos.

**Conclusão** Os critérios usados para diagnóstico, classificação e tratamento em nosso serviço seguiram os padrões estabelecidos pela literatura, e podem orientar novas pesquisas e melhorar o prognóstico local futuramente.

## Palavras-chave

- ▶ tumores de células gigantes/diagnóstico
- ▶ tumores de células gigantes/classificação
- ▶ neoplasias ósseas

## Introduction

Giant cell tumor (GCT) is an aggressive benign bone neoplasm of uncertain biological behavior. Histologically, GCT presents multinucleated giant cells dispersed within the tumor tissue, and their nuclei are similar to those of stromal ovoid and spindle cells.<sup>1</sup>

The stroma, and not the giant cells, establishes the anatomicopathological grading of a GCT. Other tumors and pseudotumors may also present with giant cells, including brown tumors resulting from hyperparathyroidism, aneurysmal bone cyst, epiphyseal chondroblastoma, osteoblastoma, and non-osteogenic fibroma.<sup>1</sup>

Giant cell tumors account for approximately 5% of primary bone tumors and 15% of benign tumors.<sup>2</sup>

They occur mainly between the third and fourth decades of life, with a slight predominance in females. Most GCTs affect the epiphyseal region of the long bones, especially the distal end of the femur, the proximal end of the tibia, and the distal end of the radius.<sup>3</sup>

The Campanacci classification is the most used in GCTs, and it divides them into three grades according to the biological behavior, the radiographic appearance, and the degree of bone destruction.<sup>3</sup>

The lytic, insufflated, metaphyseal, and aggressive features of the GCT can be clearly observed in the distal radius radiograph presented in **Figure 1**, which was extracted from the handbook by Ribeiro.<sup>4</sup>

The treatment is surgical in most cases, aiming at complete tumor resection, with preservation of the bone architecture and joint function. Correction of the created defect includes techniques such as autografting, homografting, arthrodesis, unconventional endoprotheses, and cavity fill with bone cement.<sup>5</sup>

Patients with GCTs undergoing surgical procedures must be followed up on a long-term basis; most cases of local

recurrence and lung metastasis occur within three years, but there are reports of their occurrence twenty years later.<sup>5</sup>

Because of the aforementioned information, and even though GCT is a disease that has been known and discussed for a long time, clinical and epidemiological data on this specific tumor are lacking on the regional casuistry of the state of Piauí, Northeastern Brazil. Thus, the present study aims to evaluate the treatment of patients with GCT of bone from 2009 to 2019 in a philanthropic hospital and determine



**Fig. 1** Anteroposterior radiograph of the wrist showing a lytic injury at the distal metaphyseal region of the radius, diagnosed as a giant cell tumor. Case from the Orthopedic Oncology Outpatient Clinic. Extracted from Ribeiro.<sup>4</sup>

its regional clinical and epidemiological profile to enrich the Brazilian data set and compare our findings with those of the existing literature. This will show if the criteria used in our service and our findings are consistent with those of other protocols.

## Casuistry and Methods

The present is an observational, cross-sectional, and analytical study, with retrospective data collection, a quantitative approach, and no interference by the researcher. Data collection was performed through the evaluation of the medical records from the Medical and Statistical Archive Service (Serviço de Arquivo Médico e Estatística, SAME, in Portuguese) of a philanthropic hospital regarding 49 patients with GCT treated from 2009 to 2019. The data collected included the following: patients' gender, age, degree on the Campanacci classification, anatomical tumor site, presence of lung metastasis, presence of pathological fractures secondary to the tumor, type of surgery, type of cavity filling, adjuvant treatment, recurrence rate, and previous use of denosumab.

We inserted the data on Microsoft Excel (Microsoft Corp., Redmond, WA, United States) spreadsheets, which were later exported and analyzed using the R statistical software (R Foundation for Statistical Computing, Vienna, Austria), version 4.0.3.

Contingency tables characterized the patient sample according to sociodemographic and epidemiological variables. The qualitative and quantitative variables were expressed as absolute and relative frequencies and mean  $\pm$  standard deviation respectively.

For the bivariate analysis, the Fisher exact test verified the hypothesis of an association regarding recurrence, clinical variables, and surgical modality. The tests assumed a significance level of 5% and bilateral hypotheses.

The procedures described followed the ethical research principles of resolution no. 466/12 of the Brazilian National Health Council, assuring confidentiality, anonymity, and non-use of information to the detriment of third parties; the data was used only for the purposes of the present research. Participation only occurred after the patients read and signed an informed consent form containing all the information relevant to the study. The institutional Ethics in Research Committee approved the project under opinion n° 4.362.505 and Certificate of Presentation for Ethical Assessment (CAAE) n° 36501420.5.0000.5214.

Electrofulguration used a power of 80 in the coagulation (COAG) mode, following our standard procedure.

The denosumab protocol consisted of the administration of 120 mg on days 0, 15, and 30 as "loading doses." Follow-up was based on local improvement, that is, pain relief, radiographical observation of calcifications/cortical neoformation, and gain in range of motion. Patients with little response to the initial protocol received monthly doses of 120 mg with laboratory and radiographic follow-up until reaching the ideal conditions for surgery. All patients underwent surgery.

**Table 1** Distribution of frequencies and descriptive measurements of the sociodemographic and clinical variables

Variables	N	%
<b>Gender</b>		
Male	22	44.9
Female	27	55.1
<b>Age</b>		
< 20 years	1	2.0
20 to 39 years	26	53.1
40 to 60 years	18	36.7
> 60 years	4	8.2
<b>Campanacci classification</b>		
Grade I	0	0
Grade II	15	30.6
Grade III	34	69.4
<b>Anatomical site of the tumor</b>		
Distal femur	10	20.4
Proximal femur	2	4.1
Fibula	3	6.1
Distal humerus	2	4.1
Proximal tibia	15	30.6
Distal tibia	1	2
Distal radius	6	12.2
Metacarpus	2	4.1
Proximal humerus	3	6.1
Carpus	1	2
Third finger of the right hand	1	2
Fourth finger of the right hand	3	6.1
<b>Pathological fracture secondary to the tumor</b>		
Yes	1	2.0
No	48	98.0
<b>Pulmonary metastasis</b>		
Yes	2	4.1
No	47	95.9

## Results

There were 49 medical records from patients with GCT treated at a philanthropic hospital from 2009 to 2019. The data analyzed included clinical and sociodemographic variables (**Table 1**), treatment modality (**Table 2**), and recurrence rates (**Tables 3 and 4**).

## Discussion

The epidemiological profile is consistent with the literature.

Patients undergoing an intralesional surgical procedure received intraoperative adjuvant electrofulguration and

**Table 2** Distribution of frequencies according to variables pertaining to the therapeutic modality

Variables	N	%
<b>Type of surgery</b>		
<b>Intralesional</b>	<b>34</b>	<b>69.4</b>
Grade II	15	30.6
Grade III	19	38.8
<b>Marginal</b>	<b>13</b>	<b>26.5</b>
Grade II	0	0
Grade III	13	26.5
<b>Amputation</b>	<b>2</b>	<b>4.1</b>
Grade II	0	0
Grade III	2	4.1
<b>Type of cavity filling</b>		
Bone cement	34	69.4
No filling	15	30.6
<b>Adjuvant therapy</b>		
Electrofulguration	34	69.4
None	15	30.6
<b>Use of denosumab</b>		
Yes	8	16.3
No	41	83.7
<b>Denosumab indication</b>		
Cytoreduction to facilitate surgery	8	100%

cavity filling with methyl methacrylate. Several other services use the technique described by Camargo et al.<sup>1</sup> in 1972; at our service, we call it the “Camargo technique” after its creator.

The Campanacci classification guided the choice of local therapy as reported by De Carvalho Diniz Ferraz et al.<sup>6</sup>

All patients presenting grade-II GCTs underwent intralesional surgery with electrofulguration and cavity filling with

**Table 4** Presence of recurrence according to the clinical variables and surgical modality

Variables	Recurrence		Total	p-value
	Yes – n (%)	No – n (%)		
<b>Gender</b>				
Male	5 (22.7)	17 (77.3)	22	0.440 <sup>a</sup>
Female	3 (11.1)	24 (88.9)	27	
<b>Campanacci classification</b>				
Grade II	2 (13.3)	13 (86.7)	15	1 <sup>a</sup>
Grade III	6 (17.6)	28 (82.4)	34	
<b>Surgery type</b>				
Intralesional	7 (20.6)	27 (79.4)	34	0.406 <sup>a</sup>
Marginal	1 (6.7)	14 (93.3)	15	
<b>Site</b>				
Proximal tibia	4 (26.7)	11 (73.3)	15	0.227 <sup>a</sup>
Others	4 (11.8)	30 (88.2)	34	

Note: <sup>a</sup>Fisher exact test.

methyl methacrylate. Among the 34 patients with grade-III GCTs, 13 were submitted to a marginal procedure and 2, to limb amputations; the remaining 19 patients underwent an intralesional resection followed by electrofulguration and cavity filling with methyl methacrylate. This is the current protocol of the Orthopedics Service of our hospital, and it is consistent with that of Klenke et al.<sup>7</sup> Most surgeons use intralesional resection for Campanacci grade-I and -II injuries and en bloc resection followed by reconstruction for grade-III injuries. Maybe the type of resection used in our cases was more susceptible to recurrence, which may have justified the need for a more aggressive approach for grade-III GCTs.

The intralesional surgery presented the highest rate of recurrence, with seven affected patients; only one patient

**Table 3** Data from patients with recurrent disease

#	Age (years)	Gender	Time until recurrence (months)	Campanacci classification	Adjuvant therapy	Type of surgery	Use of denosumab	Tumor location
1	34	Male	14	Grade III	Fulguration	Intralesional	No	Proximal tibia
2	33	Female	44	Grade III	Fulguration	Intralesional	No	Distal femur
3	28	Male	50	Grade II	Fulguration	Intralesional	No	Distal femur
4	51	Female	38	Grade III	Fulguration	Intralesional	No	Proximal tibia
5	31	Male	7	Grade III	Fulguration	Intralesional	No	Proximal humerus
6	49	Male	21	Grade III	None	Marginal	No	Proximal tibia
7	47	Male	6	Grade II	Fulguration	Intralesional	No	Fibula
8	52	Female	14	Grade III	Fulguration	Intralesional	Yes	Proximal tibia

who underwent marginal surgery had GCT recurrence. The anatomical site with the highest recurrence rate was the proximal end of the tibia, with four patients. ►Table 4 shows the lack of statistically significant associations among the variables and the presence of recurrences ( $p > 0.05$ ). The recurrence rate was of 16.3%, with a mean time until relapse of 24.2 months, and a standard deviation of 17.4 months; these findings are consistent with those of Manaster and Doyle,<sup>8</sup> who reported a local recurrence rate of GCT in the first 3 years after treatment of 25% in a large series. Of the 14 patients treated from 2017 to 2019, 3 had recurrences to date, while the others remain in this period of increased risk for early relapse. We will follow them up in future studies.

Regarding the therapeutic modality, the recurrence rate was higher in subjects undergoing intralesional surgery (7 out of 34 patients) in comparison to marginal surgery and amputation (1 out of 15 patients). These data are consistent with those of Reckling et al.<sup>9</sup> and McGrath,<sup>10</sup> who reported that the incidence of GCT recurrence relates to the treatment provided, being higher in patients undergoing curettage with or without bone grafting and significantly lower after segmental resection.

Eight patients received denosumab preoperatively for tumor cytorreduction to facilitate surgery, with good therapeutic response. The preoperative use of the human monoclonal antibody denosumab in advanced GCT prevents tumor osteolysis and enables the performance of a more conservative surgery.<sup>11</sup> The initial protocol consisted of 3 administrations of 120 mg with an interval of 15 days, followed by clinical and laboratory tests and radiographic reassessment. Even though our sample is small, all cases presented a good response, and denosumab helped the surgical procedure. Only one patient required a monthly administration after the initial protocol. This subject had a very extensive lesion in the distal metaphyseal region of the humerus on the dominant side, so we continued the monthly treatment with 120 mg for 10 months with strict clinical, laboratory, and radiographic follow-up. Next, the patient underwent an intralesional resection surgery with electrofulguration and no use of orthopedic cement.

As for the local prognostic factors, the Campanacci classification helped guide and select the therapy. Denosumab was important in cytorreduction, even though the series was small. The careful choice of the type of surgery is critical because GCT relapses are frequent.

## Conclusion

The clinical and epidemiological data, as well as the criteria for diagnosis, classification, and treatment used in our service were consistent with those of the literature. The Campanacci classification and its correlation with the type of surgery and previous use of denosumab were important for the treatment of GCT, and they can guide further research and improve local prognosis in the future.

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### Conflict of Interests

The authors have no conflict of interests to declare.

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