International Journal of Sciences: Basic and Applied Research (IJSBAR)

ISSN 2307-4531
(Print & Online)

http://gssrr.org/index.php?journal=JournalOfBasicAndApplied

Clinical Characteristics for Predicting Recurrency in Giant Cell Tumor of Bone

Aisyah Ameliah[a]*, Upik A. Miskad[b], Muhammad P. Johan[c], Ni Ketut Sungowati[d], Andi A. Zainuddin[e], Djumadi Achmad[f]

[a,b,d,f]*Department of Pathology Anatomy, Hasanuddin University, Makassar, Indonesia*

[c]*Department of Orthopedic and Traumatology, Faculty of Medicine, University of Hasanuddin, Makassar, Indonesia*

[e]*Department of Public Health, Hasanuddin University, Makassar, Indonesia*

[a]*Email: aisyah87.md@gmail.com*

Abstract

Giant Cell Tumor of Bone is classified as benign tumor with unpredictable biological behaviour. Recurrency and metastasis of GCTB could be found in this benign tumor. Many studies reported risk factor for recurrency of GCTB. This study is aimed to determine clinical factors for predict the recurrency in the giant cell tumour of the bone (GCTB). We collected clinical data of GCTB, included age, gender, location of tumor, radiographic, histopathological examination, then we classified GCTB samples into 3 groups, primary, recurrent, and metastatic based on the clinical and histopathological examination. From 52 samples, there were 34 samples of primary GCTB, 7 samples of recurrent GCTB or 13,5%, and 11 samples of GCTB metastatic or 21,1% from all samples GCTB. The incidens of recurrency was higher when the tumor destructed the cortex (Campanacci Grade 3), the location was in manus, and the intervention was curretage. There was a statistical significant difference recurrency between tumor location in manus and other locations ($p<0,05$). Also, there was siginificant difference recurrency between wide excision and curretage ($p<0,05$). We concluded that the clinical characteristics that could be predictors for recurrency are tumor location and method of surgery.

Keywords: GCTB; recurrency; giant cell tumor of bone; clinical characteristics.

---

* Corresponding author.

1. Introduction

Giant cell tumor of bone (GCTB) is primary bone tumor, also known as 'conventional giant cell tumour of bone' or 'osteoklastoma'. GCTB was first introduced by Cooper and Travers in 1818 as a benign neoplasm and accounts for 3–8% of primary bone tumors in Western nations, however it is more common in East and South-East Asia, accounting for 20% of primary bone tumors [1,2,3]. Although classified as a benign but locally aggressive primary bone tumor, it has tendency for local recurrency, malignant transformation can happen in 10%, and also in 1-4% cases, pulmonary metastatic is found. GCTB is most commonly found in 20–40 year old, it commonly occur around the knee, but also rarely can found in vertebrae. GCTB is found at the epiphysis of the long bone and can extend to metaphysis [1,4,5,8]. Histopathologically, GCTB is divided into benign and malignant, and it is consist of three cell types: macrophage-like round cells, reactive osteoclast-like multinucleated giant cells, and neoplastic fibroblast-like spindled stromal cells [6,7,8]. Several studies have reported that the cause of recurrency in GCTB is multifactorial and still controversial. Therefore, in this study, we are interested to know the clinicopathological characteristics that can predict the recurrency of GCTB, so we can decide the right therapy for the patient and it is expected to reduce the recurrence rate in GCTB.

2. Materials and Methods

2.1. Collection of Samples

This was retrospective study based on medical record and histopathology data. We collected fifty two samples that have been diagnosed as Giant Cell Tumor of Bone. We used total sampling method, then we classified as benign and malignant GCTB. Benign GCTB consist of primary GCTB, recurrent GCTB, and metastasis based on medical records and histopathological examination during 2016 until March 2021 from three places, that are Anatomical Pathology Laboratory of Hasanuddin University Hospital, Wahidin Sudirohusodo Hospital, and Sentra Diagnostik Patologia Laboratory in Makassar. Incomplete medical records and incomplete histopathological preparats were excluded.

2.2. Data Processing

The data were processed using descriptive statistical techniques and also processed using analyzed statistical technique that perfomed by SPSS 20 for Windows software. The clinical characteristic that influencing recurrence was classified based on gender, age, tumor location, Campanacci Grading, surgical methods, histopathological examination, recurrence, and metastasis GCTB. Correlation between clinical features and recurrency of GCTB were performed using Chi-square test.

3. Results

Fifty two samples were evaluated in this study. The distribution of GCTB were found in Table 1. More than half of patient were between 21-40 years old. For about 59,6 % patient were male. Most of the cases is graded by Campanacci Grade III. GCTB was found 23,1% in distal radius, followed by distal femur in 21,2%, proximal tibia 13,5%, manus 9,6%, proximal humerus, vertebra , and proximal femur 3,8% and other site found as

much 21,2%. There were 26 samples or 50,0% of GCTB that interveted by wide excision, same with wide excision, the other surgical method, that was curretage, also treated in 50 samples or 50,0% of GCTB. Recurrency that found in this studies was 13,5%, with duration of recurrency <1 year was occur in 2 patients, 1-2 year occur in 4 patients and >2 year in 1 patient. Metastatic rate was fairly high, that was 21,1%. There was malignant transformation in 3 samples or 5,8%.

Table 1: Distribution of GCTB based on Demographic and Clinicohistopathological Features

Demographic :	**n (%)***
Age :	
< 20 years	1 (1,9)
20-40 years	30 (57,7)
> 40 years	21 (40,4)
Sex :	
Male	31 (59,6)
Female	21 (40,4)
Clinical Features:	
Campanacci Grading:	
I	1 (1,9)
II	3 (5,8)
III	48 (92,3)
Location:	
Distal Radius	12 (23,1)
Distal femur	11 (21,2)
Proximal Tibia	7 (13,5)
Manus	5 (9,6)
Proximal humerus	2 (3,8)
Vertebra	2 (3,8)
Proximal femur	2 (3,8)
Other Site	11 (21,2)
Surgical Methods:	
Wide Excision	26 (50,0)
Curretage	26 (50,0)
Histopathology examination:	
Benign	49 (94,2)
Malignant	3 (5,8)
Duration of Recurrence:	
<1 year	2 (28,6)
1-2 year	4 (57,1)
>2 year	1 (14,3)
Primary	31(59,6)
Recurrent	7 (13,5)
Metastatic	11 (21,1)

Table 2 showed the correlation between clinicohistopathological features and the recurrency of GCTB. Based on location, there was a significant differences statistically with p value that we obtained was 0,014. We also found that there was a significant difference between surgical methods and the recurrency rate with p value 0,01. Recurrence have no correlation with age (p: 0,656), gender (p: 0,104), Campanacci grading (p: 0,547), and histopathological examinations (p: 1,000).

Table 2: Correlation between Clinicohistopathological Features and Recurrency of GCTB

Clinical Features :	**p-value**
Age :	0,656
< 20 years	
20-40 years	
> 40 years	
Gender :	0,104
Male	
Female	
Campanacci Grading:	0,547
I	
II	
III	
Location:	0,014*
Manus	
Other Site	
Surgical Methods:	0,01*
Wide Excision	
Curretage	
Histopathological Examination:	1,000
Benign	
Malignant	

The insidens of recurrency in GCTB based on Campanacci Grade, location, and surgical method was shown in table 3. Based on Campanacci Grading, insidency rate of recurrency was higher in Grade III,with a rate 14,6%. From location, we could see the recurrency rate is higher when GCTB arise in manus that other location, with recurrency rate up to 60,0%. GCTB that is intervened with curretage have a tendency to recurrence up to 27%, and we found that there were no recurrence GCTB when it is intervened with wide excision.

Table 3: The insidens of recurrency in GCTB based on clinical characteristic

Clinical Characteristic	**Recurrent**	**Non-recurrent**	**Total**	**Incidens of recurrency**
Campanacci Grade				
I	0	1	1	0%
II	0	3	3	0%
III	7	41	48	14,6%
Location				
Manus	3	2	5	60,0%
Other location	4	43	47	8,5%
***Surgical Method*:**				
Wide Excision	0	26	26	0%
Curretage	7	19	26	27%

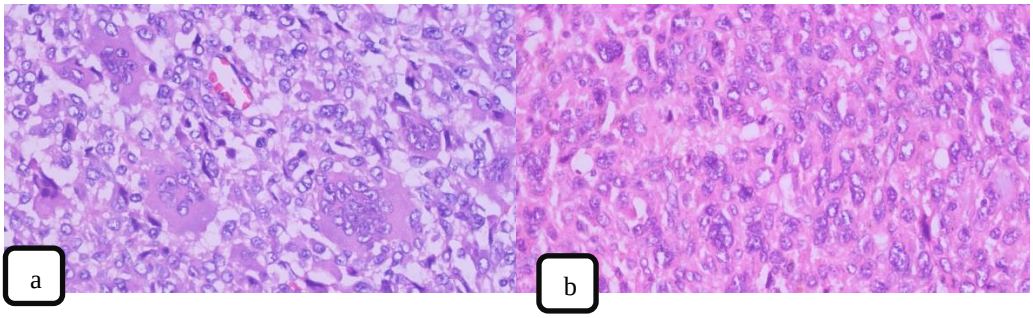

Figure 1: Histopathological Examinations. (a) Benign GCTB; (b) Malignant GCTB (x400)

4. Discussion

GCTB is the most common primary bone tumor, however its incindence is varied in different series. It is reported that incidence of GCTB is higher in South East Asian than other regions around the world [9]. Although categorized as benign tumor by histopathology, GCTB shows different biological behavior, it is an unpredictable tumor because the possibility of local recurrence is quite high and the possibility of metastases can also occur in this benign case. The tendency to have local recurrent and metastasis in this benign tumor makes it an interesting subject to study. In this study, from 52 patients, 30 patients or 57,7% were in 20-40 years old. Its due to GCTB mostly occur in skeletally matured bone. GCTB occur in male as many as 31 patients, this is different from some references [5,7] who reported that GCTB was more common in female with a ratio of 1.2:1, the theory that explain this is female has faster bone maturation than male. However, researcher from

India [4] and from Indonesia who used samples from Bandung [10] also reported that the incidence rate was higher in male than female. Our study obtained that there were 48 patients or 92,3% with Campanacci grade 3, there were 3 patients with Campanacci grade 2, and there was only 1 patients with Campanacci grade 1. The patient's delay in checking up could be the reason for the tumor the higher grade, therefore the right surgical method is needed to remove the tumor and maintain joint function. However, in this study, we revealed recurrency was not correlated with Campanacci Grading with p value 0,547. In several studies [11,12,13,14], Campanacci Grading is reported can be used as a prognostic marker to see the possibility of recurrence in GCTB patients. However, in other research [15,16] have revealed that the recurrency of GCTB is not associated with Campanacci grade, and the surgical method is the major factor that influence recurrency after operative [15]. GCTB was found more common in the distal radius in 12 patients, then in the distal femur in 11 patients and in the proximal tibia in 7 patients. In manus, there were 5 patients, and 3 of them had recurrence. Compared with other location, GCTB in manus have more higher incidens to recur, that is 60,0% with p value 0,014. It caused by tumor cells are difficult to clean at the time of surgery. This finding is in line with previous study [10] that reported that GCTB was also higher in distal radius. In this study, there were 26 patients who intervened with curettage and there were 26 patients who intervened with wide excision. For the recurrence rate, it was found that patients treated with curettage were more likely to experience recurrence with a recurrence rate of 27%. We also tested statistically the correlation between recurrence and surgical method, and obtained p value: 0.01. So it suggested that there was a significant correlation between the method of surgery and the rate of recurrence. The authors in [11,15] revealed that surgical method is correlated with recurrence. When curretage was performed on the patient, the likelihood of recurrence was higher than when we performed wide excision, but the side effect of wide excision was greater, namely joint dysfunction. Histopathologically, there are two types of GCTB, namely benign and malignant. In this study, almost all samples were benign GCTB, ie 49 samples, and 3 samples were malignant GCTB. However, histopathology did not show the biological behavior of GCTB, benign GCTB was found to have recurrence and metastasis, as was found in this study, namely 7 samples or 13.5% benign were found to have recurrence and 11 samples or 21.1% had lung metastases. The highest duration of recurrence was found at 1-2 years postintervention. This is in line with other studies [16] that reported GCTB was not correlated with histopathological examinations. In this study, we found interesting facts that the metastatic rate is higher than other studies have revealed, with a high involvement of the distal radius. The other interesting fact that is more that half of patients (92,3%) were in Campanacci 3 at the time of presentation. It was found that the clinical characteristics that had a significant correlation with recurrence were the location of the tumor and the method of surgery. Meanwhile, age, gender, Campanacci and histopathological examination had no correlation with the recurrence rate. The tendency for recurrence is higher if the patient presents with Campanacci grade 3, the location of the tumor is on the manus, and the procedure performed on the patient is curettage. The limitations of this study was the medical records were taken from January 2016 until March 2020 so that the time for follow up and the numbers of samples were limited.

5. Conclusion

Clinical characteristics that could be factors that predict recurrency of GCTB are tumor location and surgery methods. The occurrence of recurrence is higher when the tumor destruct the cortex (Campanacci Grade 3), the location is in manus, and the intervention is curretage.

References

[1]. Lin, F., et al., "The epidemiological and clinical features of primary giant cell tumor of bone around the knee: A report from the multicenter". Journal of Bone Oncology, vol. 5, pp.38–42. 2016.

[2]. M. A. Siddiqui, C. Seng, & M.H Tang,"Risk factors for recurrence of giant cell tumours of bone."Journal of Orthopaedic Surgery, vol. 22, no.1, pp.108-110. 2014.

[3]. M.H. Zheng, et al., "The histogenesis of giant cell tumour of bone: a model of interaction between neoplastic cells and osteoclasts". Histol and Histopathol, vol.16, no.1,pp. 297-307, 2001.

[4]. K. Gunasegaran, M.N.S.B. Irawan, A. Yantiasetiasti, "Epidemiology of Giant Cell Tumor in Dr. Hasan Sadikin General Hospital Bandung from 2010-2013." Althea Medical Journal, vol. 3, no.2, pp.244-47, 2016.

[5]. D.M. Fletcher, J. A. B., Pancras C.W. Hogendoorn, F. Mertens. WHO Classification of Tumours of Soft Tissue and Bone (4 ed.). France: International Agency for Research on Cancer. 2013. pp. 319–22

[6]. M. Werner. "Giant cell tumor of bone: morphological, biological, and histogenetical aspects". International Orthopaedics, vol.30, pp. 484-9, 2006.

[7]. B. J. Noh, & Y. K. Park, "Giant cell tumor of bone of bone: updated molecular pathogenesis and tumor biology." Human Pathology. vol.81, pp. 1-8, 2018.

[8]. A. S. Singh, N.S. Chawla, & S. P. Chawla, "Giant-cell tumor of bone: treatment options and role of denosumab". Biologics : targets & therapy, vol.9, pp. 69–74, 2015.

[9]. X. Niu, et al., "Giant cell tumor of the extremity retrospective analysis of 621 Chinese patients from one institution". J Bone Joint Surg Am, vol.94,no.5, pp. 461–7, 2012.

[10]. K.C. Saikia, S.K. Bhuyan, M. Borgohain, S.P. Saikia, A. Bora, F. Ahmed, "Giant cell tumour of bone: an analysis of 139 Indian patients". J Orthop Sci, vol.16, no.5, pp.581-8, 2011.

[11]. N. Lujic, J.Sopta, R.Kovacevic, V.Stevanovic, R. Davidovic, "Recurrence of giant cell tumour of bone: role of p53, cyclin D1, β-catenin, and Ki67". International Orthopaedics, vol. 40(11), pp.2393-2399, 2016.

[12]. G.H. Prosser, K.G. Baloch, R.M. Tillman, S.R. Carter, R.J. Grimer,"Does curettage without adjuvant therapy provide low recurrence rates in giant cell tumours of bone?" Clin Orthop Relat Res, vol.435, pp. 211–8, 2005.

[13]. A. Takeuchi, H. Tsuchiya, X. Niu, T.Ueda, D.G. Jeon, E.H. Wang, Y.K. Kang, "The prognostic factors of recurrent GCT: a cooperative study by the Eastern Asian Musculoskeletal Oncology Group". J Orthop Sci, vol.16(2), pp.196-202, 2011.

[14]. Y.H. Han, et al., "Expression of CD147, PCNA, VEGF, MMPs and their clinical significance in the giant cell tumor of bone of bones". Int J Clin Exp Pathol, vol. 8(7), pp. 8446-8452, 2015.

[15]. D.D. Cheng, T. Hu, H.Z. Zhang, J. Huang, J., & Q.C. Yang, "Factors Affecting the Recurrence of Giant cell tumor of bone of Bone After Surgery: A Clinicopathological Study of 80 Cases from a Single Center". Cell Physiol Biochem, vol.36(5), pp. 1961-1970, 2015.

[16]. X. Zhou, X.Z.Liu, G.T.Fan, S.J.Wu, J.N. Zhao, X. Shi, "Expression of Matrix Metalloproteinase-9 and CD34 in Giant Cell Tumor of Bone". Orthopaedic Surgery, vol.8 (2), pp. 220–225, 2016.