International Journal of Healthcare Sciences ISSN 2348-5728 (Online)
Vol. 8, Issue 2, pp: (342-346), Month: October 2020 - March 2021, Available at: www.researchpublish.com

CLINICOPATHOLOGY PROFILE OF GIANT CELL TUMOR OF BONE IN RSUP SANGLAH 2015-2019

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Abstract: **Giant cell tumors of bone (GCTB) are kind of benign tumors with potential of aggressive and capability to metastase. GCTB is more common in Asia and occur around the knee. In Asia, most cases shown in men. Curettage alone has been the standard treatment for GCTB, but it has been associated with a relatively high risk of local recurrence ranging up to 35–40%. The study was cross sectional conducted with retrospective descriptive design. Samples of 38 patients diagnosed with Giant Cell Tumor of Bone (GCTB) at the Sanglah Hospital Denpasar Medical Record Installation, Bali for the period 2015-2019 were selected based on inclusion and exclusion criteria. Data were analyzed using SPSS software to obtain distribution, frequency based on age, sex, tumor location, mitotic activity, recurrency. The case of giant cell tumor of bone (GCTB) of bone at Sanglah General Hospital**

Denpasar Bali in 2015-2019 was 38 people, the patient characteristics were mostly women (65,8%) with an age range dominated by the 2nd to 4th decade or life (47.4%). Characteristics of GCT of bone indicate the location of the distal femur is the most common case (26,3%) with mitotic activity of 1 and 3 per 10 hpfs and only 5.3% of cases of recurrent GCTB. It was concluded that the case of gian cell tumor of bone (GCTB) of bone at Sanglah General Hospital Denpasar Bali in 2015-2019 mostly women (21-40) and the location of the distal femur is the most common case with mitotic activity of 1 and 3 per 10 hpfs and only 5.3% of cases of recurrent GCTB.

Keywords: **clinicopathology, recurrenct, giant cell tumor of bone (GCTB).**

1. INTRODUCTION

Giant cell tumors (GCT) are some kind of benign tumors with potential of aggressive behaviour and capability to metastase. GCT represents about 5% of all main bone tumors with the metastase rate is around 1%-9%. Approximately half of these lesions occur at the age of 30 to 40.[1] GCT of bone (GCTB) is one of the GTCs that is locally aggressive composed of mononuclear cell's sheets, affecting the metaphysis of long bones primarily. Recently, the incidence was estimated at between 1.03-1.33 per million per year in the registry of Australia, Japan and Sweden. Median age of onset ranges between 20-40 years old with an equal distribution between gender, although female are slightly predominance.[2] The prevalence of GCT peaks during the 3rd decade, with 80% of cases occurring between 20 and 50 years of age. Less than 3% of cases occur before the age of 14 years, and only 13% of cases occur in patients over the age of 50 years. Most lesions develop in long bones (75%–90%), with the majority of cases (50%–65%) occurring about the knee. The three most common locations are the distal femur, proximal tibia, and distal radius, respectively. GCT may occur in association with Paget disease, most commonly in the skull, facial bones, pelvis, and spine. GCTB is more common in Asia, accounting for 20% of primary bone tumor and occur around the knee. In Asia, most cases shown in men with gender

ratio 1,27-1,77 compared to women. It has been reported that the postoperative reccrence rate is 10%-65% make it the most controversial and widely discussed bone tumors.[3]

GCTB is generally a benign tumor composed of mononuclear stromal cells and characteristic multinucleated giant cells that exhibit osteoclastic activity. It usually develops in long bones but can occur in unusual locations. The typical appearance is a lytic lesion with a well-defined but nonsclerotic margin that is eccentric in location, extends near the articular surface, and occurs in patients with closed physes, however GCT may have aggressive features, including cortical expansion or destruction with a soft-tissue component. Fluid-fluid levels, consistent with secondary formation of aneurysmal bone cysts, are seen in 14% of cases. GCT can mimic or be mimicked by other benign or malignant lesions at both radiologic evaluation and histologic analysis.[1,3] Different classifications have been proposed based on the histology, clinical and radiographic appearance, but they provide little prognostic information regarding the risk for local recurrence. Curettage alone has been the standard treatment for GCT, but it has been associated with a relatively high risk of local recurrence ranging up to 35–40%.[3] The data about recurrent GCTB in Indonesia especially in Bali have not widely established yet. To enhance the data, researcher wants to study about the clinicopatholgy characteristic of reccurent GCTB in Sanglah Central Hospital, Bali as the main centre of healthcare for Bali province.

2. MATERIALS AND METHODS

This study uses a retrospective descriptive design which aims to determine the clinocopatholigical characterisctics of recurrent Giant Cell Tumor Of Bone according to age, gender, tumor location, mitotic activity and time of recurrency based on patients from Pathology Anatomy Labaratorium RSUP Sanglah in Denpasar from the year 2015–2019. The method of choosing the sample is total sampling, where researchers choose a sample based on subjective considerations and practical, in this case the Patient Registration Logbook of patients that fit into the inclusion criteria based on age and time period and the diagnosis of Giant Cell Tumor of Bone with corresponding available data regarding clinical manifestation and treatment. The independent variabke for this study is to determine the clinocopathological characteristics of recurrent Giant Cell Tumor of Bone depending on age of patients, sex of patients, tumor location, mitotic activity and time of recurrency.

The data obtained was then anylysed using the SPSS programme and will be analysed descriptively. Result will be showed as tables and graphics. This research has received ethical eligibility permission from the Research Ethics Commission (KEP) of the Faculty of Medicine, Udayana University with letter number B/8449/UN14.2.2.V.1/ PT.01.04/2020.

3. RESULTS AND DISCUSSION

Patients diagnosed with Giant Cell Tumor of Bone (GCT) at the Sanglah Hospital Denpasar Medical Record Installation, Bali for the period 2015-2019, based on the inclusion and exclusion criteria, there were 38 peoples. The entire sample has a different line for each variable.

Characteristics of Respondents

This study showed that more than half of the incidence of GCT of bone was suffered by women, namely 25 cases (65.8%) as shown in table 5.1, where if it is formed into the ratio of cases in men and women reaches 1:2. A similar ratio was also found in previous studies, where the majority of GCT of bone patients were female.[4] Similar results were also obtained in a study conducted in the Netherlands, namely the incidence of GCT of bone which is more common in women with a male: female ratio reaching 1:1.38.[2] The incidence of GCT of bone in women was reported to reach 51.5% to 60% in the previous literature.[5]

Table 1: Gender Characteristics of Patients

Gender	Frequency	Percent (%)	Valid Percent	Cumulative Percent
Male	13	34.2	34.2	34.2
Female	25	65.8	65.8	100.0
Total	38	100.0	100.0	

Characteristics of Respondents Based on Age

This study shows the incidence of GCT in the 2nd to 4th decade (adolescents) as many as 18 cases (47.4%) as shown in table 5.2. This finding is consistent with the statement in the previous article which states that the age range with the highest incidence of GCT of bone is generally 20 to 40 years, and is very rare in children and <10% of cases are found at> 65 years of age.[6] Other previous studies have also strengthened the suitability of the results, where the 20-24 year age range has the highest incidence of GCT of bone cases.[2] The majority of the incidence of GCT of bone in the 2nd decade was also reported by a study conducted by Kafchitsas et al., namely 28 years with a patient population aged 13-56 years.[4] Meanwhile, research conducted at the Cipto Mangunkusumo National General Hospital showed that the highest incidence was found in patients in the 3rd decade but still in the age range of 20-40 years, the high incidence in this age range is related to bone maturation, but other detailed mechanisms cannot be explained.[7]

Table 2: Patient Age Characteristics

Age	Frequency	Percent (%)	Valid Percent
0-20	15	39.5	39.5
21-40	18	47.4	47.4
>40	5	13.1	13.1
Total	38	100	100

Characteristics of Giant Cell Tumors (GCT) of Bone based on Location, Mitotic Activity and Recccurency

This study showed the distribution of GCT of bone was mostly found in the long bones of the lower extremities, namely the femur, which is the distal part, namely 10 cases (26.3%). In addition, this study also shows the distribution of GCT of bone in the axial area, namely the illiac and sacrum. Similar results were also reported by previous research in the Netherlands which stated that the highest

incidence of GCT of bone was in the lower extremities, namely the femur by 35%.[2] This is in line with previous studies which stated that the majority of cases of GCT of bone involved the distal area of the femur, which were 17 out of 38 cases.[4] Apart from the extremities, cases of GCT of bone can also be found in the axial parts of the body such as the illiac and sacrum.[8]

This study demonstrated cleavage or mitotic activity of GCT of bone ranging from 1 to 17 per 10 hpfs with 1 and 3 per 10 hpfs as the highest numbers counted at 8 cases (21.1) each. In addition, the lowest number of mitosis is 6 and 17 per 10 hpfs, which is 1 (2.6%). Previous studies showed that the mean mitosis rate was 3/20 hpfs and no atypical mitosis was found.[9] Mitosis picture which is formed shows a typical type of mitotic picture with mitotic activity that can reach 20/10.[10] Although multinucleated giant cells are a distinctive cell type, these lesions have a base mononuclear stromal cell network. The formation of mononuclear cells can be oval, or spindle-shaped. In addition, GCT also has prominent mitotic activity, but rarely with cellular atypia. In contrast to the nucleus of Langerhans-type giant cells which are core located peripherally and are seen during atypical infection, multinucleate giant cells have many centrally located nuclei. The nucleus is compact and oval and contains a prominent-nucleoli and the concentration of multinucleated giant cells differs from tumor to tumor. Some cases, the tumors have many multinucleated giant cells, while others have a small number of giant cells located in the spindle-shaped vortex of the stromal cells. In about 5% of cases, the giant cells invade the small, hollow blood vessels.[11]

This study shows the incidence of recurrence in medical record data for 5 years, from 2015-2019, there were 2 cases out of a total of 38 cases or only 5.3% as shown in table 5.3. In contrast to previous studies which stated that 26% of patients experienced recurrency GCT of bone, where the sacrum and lower limb areas were the areas with the highest number of cases.[12] This can be caused by patients who stop therapy and choose to undergo traditional therapy and or seek medical treatment abroad. Other reslut showed that low rate of recurrence can be achieved if treatment for patient is selected according to histopathological exam and with a properly technique.[13] Recurrence of GCT of bone generally occurs 2-3 years after surgery/surgery. This recurrence is caused by improperly performed curettage which can cause recurrence in more than 80% of cases and and the other is due to genetics, wherein individuals with bone giant cell tumors show teleomeric association (tas) cytogenetic abnormalities.[14] Based on this, it is recommended to use thermal cauterization with 5% phenol, 70–90% alcohol, bone cement or with liquid nitrogen which aims to clean the tumor cavity walls from tumor cells that are left behind by surgery.[7] Another study states that as many as 30% of recurrent cases occur at 1 year and 3 years after the procedure with the femur and tibia as the most frequent recurrent locations.[2]

Table 3: Characteristics of Giant Cell Tumors (GCT) of Bone

Variable	Frequency	Percent (%)	Valid Percent	Cumulative Percent
Location				
Calcaneus Pedis	1	2.6	2.6	2.6
Cruris	1	2.6	2.6	5.3
Distal Femur	10	26.3	26.3	31.6
Distal Radius	8	21.1	21.1	52.6
Distal Tibia	3	7.9	7.9	60.5
Illiac	2	5.3	5.3	65.8
Phalang/digiti	5	13.2	13.2	78.9
proks Femur	4	10.5	10.5	89.5
proks Tibia	3	7.9	7.9	97.4
Sacrum	1	2.6	2.6	100.0
Mitotic activity/10 hpfs				
1	8	21.1	21.1	21.1
2	4	10.5	10.5	31.6
3	8	21.1	21.1	52.6
4	4	10.5	10.5	63.2
5	7	18.4	18.4	81.6
6	1	2.6	2.6	84.2
7	3	7.9	7.9	92.1
10	2	5.3	5.3	97.4
17	1	2.6	2.6	100.0
Recurrency				
Primary GCT	36	94.7	94.7	94.7
Recurrent GCT	2	5.3	5.3	100.0
Total	38	100.0	100.0	

4. CONCLUSION

Based on the results of the study, it was concluded that the case of giant cell tumor (GCT) of bone at Sanglah General Hospital Denpasar Bali in 2015-2019 was 38 people, the patient characteristics were mostly women with an age range dominated by the 2nd to 4th decade or life (47.4%). Characteristics of GCT of bone indicate the location of the distal femur is the most common case with mitotic activity of 1 and 3 per 10 hpfs and only 5.3% of cases of recurrent GCT.

5. RECOMENDATION

Based on the research that has been done, the following suggestions can be given, it isnecessary to do further research on the relationship between variables. The addition of other characteristics related to staging, previous control history, therapeutic data provided to improve the quality of the patient's medical record and can be used as material for further research

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