Original Article

Histopathological Evaluation of Giant Cell Tumors of Bone: An Observational Study in the Population of South West Bihar

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ABSTRACT

Background: With an estimated prevalence of 1 to 9%, Giant Cell Tumour (GCT) is the unique benign bone tumour, along with chondroblastoma, that can have distant metastases. Its biological behaviour exhibits significant variety, ranging from a latent benign to a greatly recurring and occasionally metastatic potential. Identification of various histopathological component would be crucial in predicting the clinical outcome, recurrence, and metastasis.

Aims/ objective: To identify and measure prevalence of various histopathological features of giant cell tumour of bone in a tertiary care hospital of eastern India.

Materials and Method: 50 patients of histopathologically diagnosed giant cell tumour were enrolled in this study. Cases were evaluated according to radiological features, clinical features such as age, gender, localization, recurrence, metastasis, and histopathological features including accompanying fibro-histiocytic or aneurysmal bone cyst like components. Descriptive statistics was done to obtain frequency and percentage of various demographic, histopathological, and radiological features.

Results: 88% of giant cell tumor were of long bones. Tibia (26%) and femur (24%) were most commonly involved bone. Secondary aneurysmal bone cyst like component were present in 18% of cases, coagulation necrosis in 16% and fibro-histiocytic component in 14%. Most common location in long bones were epiphyseal-metaphyseal (45.45%), metaphyseal-epiphyseal (43.18%).

Conclusion: Giant cell tumor is a benign pathology with most common location in long bone in tibia and femur, most prevalent in 20-40 years of age group and typically presents as an epiphyseal-metaphyseal, eccentric, lytic lesion with pseudo-trabeculations

Keywords: Giant Cell Tumour, Histopathology, Bone Biopsy, Radiological Feature.

INTRODUCTION

Giant cell tumour of bone (GCT) is an osteolytic tumour that typically affects young to middle-aged individuals. It typically arises in the axial skeleton, such as the spine or sacral, or in the metaphysis to epiphysis of a long bone, such as the femur or tibia.[1] Mononuclear stromal cells, mononuclear neoplastic cells, and multinucleated large cells resembling osteoclasts make up the distinctive histological hallmark of GCT.[1-2] The H3F3A and H3F3B genes encode histone H3.3, and nearly all tumours have a mutation in H3F3A p.G342. The most common variant in GCT (~90%) is H3F3A p.G34W.[2-4] The H3F3A p.G34L, p.G34M, p.G34R, or p.G34V mutation is present in minor subgroups (each <2%).[2-4]

Jaffe originally described the tumour in 1940.[5] The third and fourth decade of life are when the incidence peaks.[6,7] In the clinical setting, it is typically observed as a lytic lesion of the bone's epiphyseal area. The proximal tibia and distal femur are where it most frequently happens. A well surrounded lytic lesion overlying the epiphyseal area is typically detected radiologically. From a histopathological perspective, these tumours consist of uniformly dispersed multinuclear giant cells, macrophages, and mononuclear cells.[7]

About 20% of benign bone tumours are giant cell tumours of bone (GCT), a frequent bone disease.[8] Its local aggression sets it apart from different benign bone neoplasms. With an estimated prevalence of 1 to 9%, it is the unique benign bone tumour, along with chondroblastoma, that can have distant metastases.[9] Its biological behaviour exhibits significant variety, ranging from a latent benign to a greatly recurring and occasionally metastatic potential. Its radiological image likewise reflects this heterogeneity. From a clearly defined regional lesion to a locally invasive lesion that completely destroys the bone, it can appear radiologically as a spectrum.[10]

In a biological sense, the interaction between nuclear factor kappa-B ligand (RANKL) released by neoplastic osteoblastic cells and receptor activator of nuclear factor kappa-B (RANK) on osteoclasts is crucial for promoting the process of osteoclast development and activation, which accelerates osteolysis.[11,12]

It is believed that GCT is primarily an osteoclastogenic stromal tumour. It has been demonstrated that reactive

osteoclasts were the large cells in GCT. [13,14] It was suggested that the proliferative and neoplastic components of GCTs were the mononuclear stromal cells, and it has been documented that such neoplastic stromal cells might induce the development of osteoclasts. [15,16]

The osteoclast progenitor cells were believed to be mononuclear monocytes.[17] Rare mitotic figures may be seen in mononuclear stromal cells, but atypical mitosis is not seen. [13] Multinucleated giant cells do not exhibit mitotic figures. [7] Mononuclear stromal cells do not exhibit any significant cytologic atypia. [7,13]

Identification of various histopathological component would be crucial in predicting the clinical outcome, recurrence, and metastasis. So, this study was planned to identify and measure prevalence of various histopathological features of giant cell tumour of bone, especially accompanying fibro-histiocytic or aneurysmal bone cyst like components in a tertiary care hospital of eastern India.

MATERIALS AND METHODS

This was an observational and prospective study conducted on patients of giant cell tumour in Department of Pathology in collaboration with Department of Orthopaedics from July 2022 to June 2023. The study was conducted after obtaining written informed consent from study participants who were explained participant information sheet in their given language as per guidelines of declaration of Helsinki and Good Clinical Practice.

Sampling method: Consecutive sampling was done and all the patients of giant cell tumour fulfilling our inclusion and exclusion criteria were enrolled in the study.

Inclusion Criteria: Patients of either gender of age greater than 18 years with histopathological diagnosis of giant cell tumour of the bone were included in the study.

Exclusion Criteria: Patients with other malignancy or pathological disease of bone or with inadequate information or not willing to participate were excluded from the study.

Methodology: Cases were evaluated according to radiological features, clinical features such as age, gender, localization, recurrence, metastasis, and histopathological features including accompanying fibro-histiocytic or aneurysmal bone cyst like components.

Three types of cells were looked for in biopsy sample: [18]

- Type I cells can multiply and resemble interstitial fibroblasts. They also produce collagen. This cell is most likely the GCT tumour component. Mesenchymal stem cells and type I cells share characteristics. They have traits that point to the possibility that they are an early osteoblastic differentiation.
- Type II cells can be drawn from the peripheral circulation and are also interstitial; nonetheless, they resemble the monocyte/macrophage family. These cells are multinucleated giant cell progenitors.
- Multinucleated large cells are classified as Type III cells. They resemble osteoclasts in morphology and share many of their traits. They possess type II carbonic anhydrase and tartrate-resistant acid phosphatase, two enzymes involved in bone resorption.

Statistical Analysis: Data collected from patients with GCT were presented in tabular form using Microsoft Excel 365 and then transferred to Graph Pad version 8.4.3 for further statistical analysis. Descriptive statistics was done to obtain frequency and percentage of various demographic, histopathological, and radiological features.

OBSERVATIONS AND RESULTS

50 patients of histopathologically diagnosed giant cell tumour were enrolled in this study. Their baseline demographic is given in table 1.

Table 1: Baseline demographic and clinical characteristics of patients with GCT

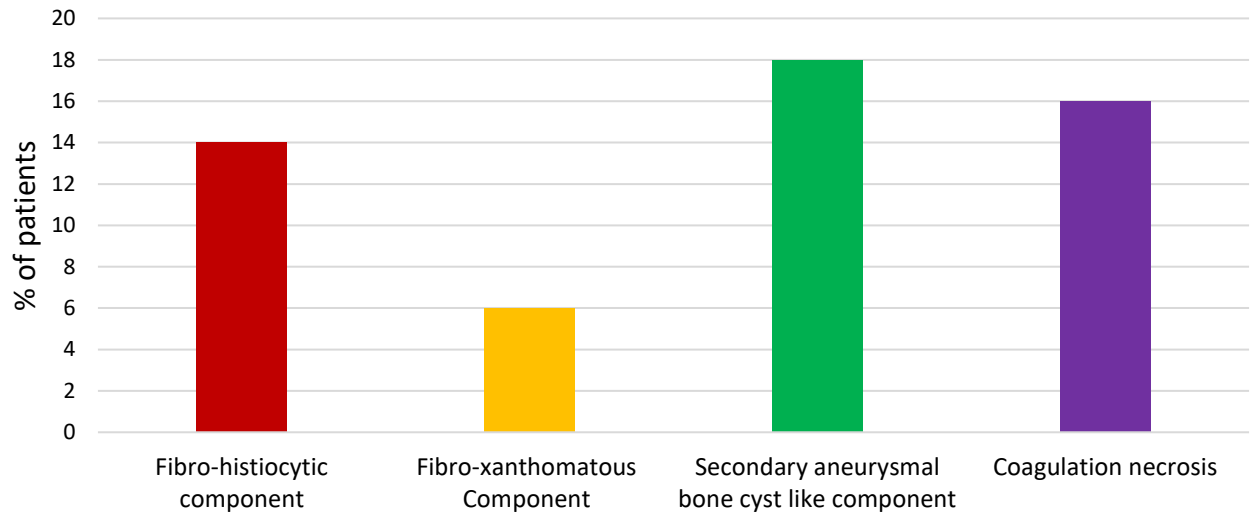
Parameters	Number of Patients	% of Patients (n=50)
Age		
18-30	20	40.00
31-40	18	36.00
41-50	6	12.00
51-60	4	8.00
>60	2	4.00
Gender		
Male	27	54.00
Female	23	46.00
Location		
Tibia	13	26.00
Femur	12	24.00
Humerus	8	16.00
Radius	7	14.00
Sacrum	3	6.00
Vertebra	3	6.00
Fibula	2	4.00
Rib	1	2.00
Ulna	1	2.00

Most of the patients (>70%) belonged to 21-40 years of age group. There was slight male preponderance. 88% of giant cell tumor were of long bones. Tibia (26%) and femur (24%) were most commonly involved bone.

Table 2: Histopathological findings of patients with GCT

Parameters	Number of Patients	% of Patients (n = 50)
Mono-nuclear stromal cells	100	100.00
Mono-nuclear monocytes	100	100.00
Multinucleated giant cells	100	100.00
Fibro-histiocytic component	7	14.00
Fibro-xanthomatous Component	3	6.00
Secondary aneurysmal bone cyst like component	9	18.00
Coagulation necrosis	8	16.00

Figure 1: Histopathological findings of patients with GCT



In all patients, characteristic areas made up of mono-nuclear stromal cells and mono-nuclear monocytes and multi-nucleated giant cells, which represent GCT, were found by taking two samples for every one centimeter of the tumor's maximum diameter. Secondary aneurysmal bone cyst like component were present in 18% of cases, coagulation necrosis in 16% and fibro-histiocytic component in 14%.

Table 3: Radiological feature of patients with GCT

Parameters	Number of Patients	% of Patients
Pseudo-trabeculations (n = 50)	31	62.00
Pathological fracture (n =50)	5	10.00
Joint involvement (n = 50)	19	38.00
Location in long bone (n=44)		
Epiphyseal-metaphyseal	20	45.45
Metaphyseal-epiphyseal	19	43.18
Epiphyseal-metaphyseal-diaphyseal	4	9.09
Metaphyseal	1	2.27
Centricity in long bone (n=44)		
Centric	17	38.64
Eccentric	27	61.36
Type of Lesion (n=50)		
Hairline sclerotic rim	22	44.00
Thick sclerotic rim	9	18.00
No sclerotic rim	7	14.00
Moth-eaten / Permeative	12	24.00

On radiological imaging, 62% patients had pseudo-trabeculations, 38% with joint involvement and only 10% with pathological fracture. Hairline sclerotic rim was found in 44% of cases. Most of the tumor in long bones were eccentric (61.36%). Most common location in long bones were epiphyseal-metaphyseal (45.45%), metaphyseal-epiphyseal (43.18%).

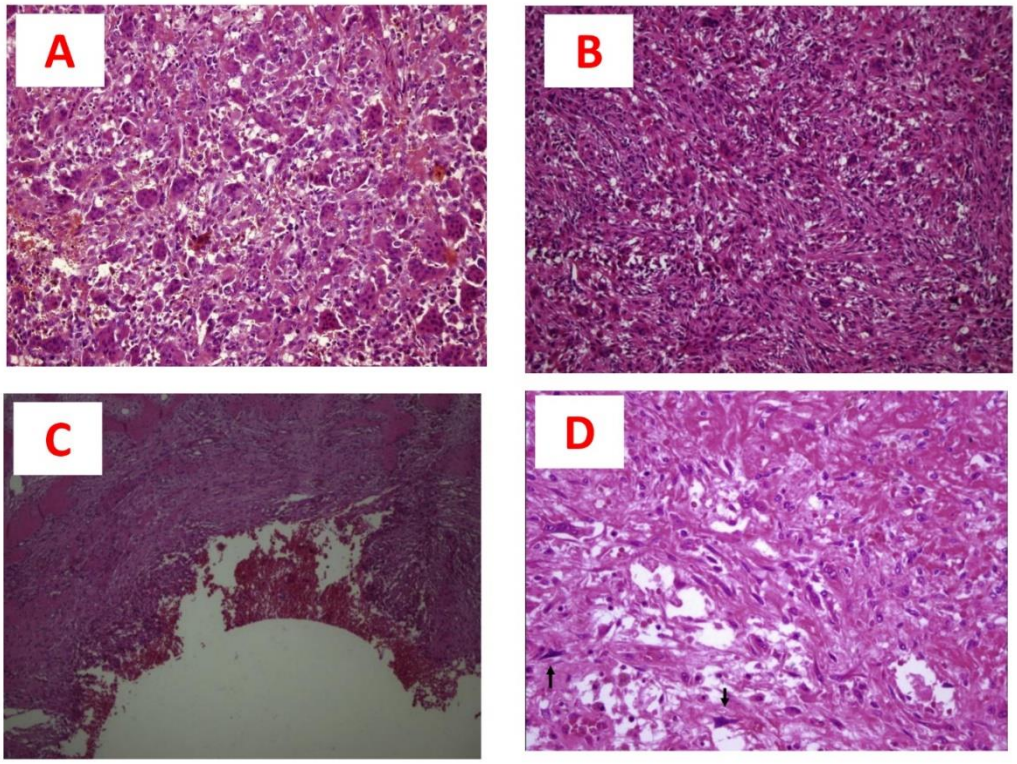


Figure 2: Histopathological slides A) Mono-nuclear cells and multi-nucleated giant cells (H-E, X 200) B) Fibro-histiocytic component (H-E, x100) C) Secondary aneurysmal bone cyst (H-E, x40 D) Necrotic areas (arrows) (H-E, x200)

DISCUSSION

A locally aggressive tumor with an erratic course is called GCT. According to reports, it is uncommon for GCT to occur in patients under the age of 20 and above the age of 55[7]. Four individuals (8% of the total) in our study were beyond the age of 55. Previous investigations have found comparable findings. [19,20]

It has been noted that non-epiphyseal GCT is incredibly unusual. [7] We have noticed a single case at metaphysis in our investigation. The most common location for the tumor in our investigation was the proximal tibia, followed by the distal femur. The distal end of the femur and the proximal end of the tibia were shown to be the most frequently affected sites in earlier studies. [6,7]

In 14% of the cases in our study, a fibro-histiocytic component was found. Hemorrhage, necrosis, fibrohistiocytic proliferation, and the creation of aneurysmal bone cysts are examples of subsequent reactive alterations that commonly obscure the clearly defined histopathologic pattern of the GCT. A differential diagnosis between benign fibrous histiocytoma and non-ossifying fibroma (NOF) should be made when fibro-histiocytic reaction becomes noticeable. In metaphysis, NOF takes place. In contrast to GCT, NOF's stroma tends to be more fibroblastic and can occasionally form a storiform pattern. Additionally, NOF's large cells are distributed more erratically. It has been noted that lipoidization, scarring, and fibro-histiocytic proliferation have formed in the end phase of reparative processes after bleeding and necrosis.[5,21] Mononuclear cell sheets are not seen in wide sheets in benign fibrous histiocytomas.[22]

In 18% of the cases in our analysis, there was a secondary aneurysmal bone cyst (ABC) like component. In GCT, aneurysmal bone cyst-like regions are often found. Particularly substantial portions of aneurismal bone cysts can be mistakenly identified as GCTs. Giant cells are dispersed unevenly and are smaller in ABC. The stroma of solid ABC tends to be more fibrotic compared to GCT.[22] Except in one instance, areas exhibiting typical GCT were found with additional sampling. In this instance, the tumor displayed typical solid type ABC regions, making a firm diagnosis impossible to make and ruling out GCT.

In a traditional GCT, necrosis either with or without bleeding may occasionally be seen. Mononuclear stromal cells may exhibit focal cytologic atypia next to the necrotic regions, which could be mistaken for cancer.[6] Nonetheless, the absence of aberrant mitosis corroborates the benign character of these modifications. Despite the fact that 8 of the instances in our study had necrosis, none of the cases had any obvious cytologic atypia or abnormal mitosis.

It is important to distinguish giant-cell rich osteosarcoma from GCT. Nuclear pleomorphism, aberrant mitotic figures, and malignant osteoid development are hallmark features of giant-cell rich osteosarcoma.[23] Only one patient, a 26-year-old woman with metaphysis of the fibula who was examined in our institute during this 20-year period and whose histological results showed these abnormalities, was diagnosed as "osteosarcoma rich in giant cells." Soft tissue invasion was also present in this tumor. Since no malignant osteoid development or abnormal mitosis had been found, the diagnosis of a giant-cell rich osteosarcoma in one patient was modified to GCT.

CONCLUSION

Giant cell tumor is a benign pathology with most common location in long bone in tibia and femur, most prevalent in 20-40 years of age group and typically presents as an epiphyseal-metaphyseal, eccentric, lytic lesion with pseudo-trabeculations and this pattern is most prevalent in a patient with closed physis growth plates. More sampling is required for tumors with noticeable fibro-histiocytic and aneurysmal bone cyst-like components in order to identify distinctive regions indicative of giant cell tumors.

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