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CASE SERIES

# Denosumab in Giant Cell Tumour of Bone - A Case Series with Review of Literature

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## Abstract

**Introduction:** Giant Cell Tumour of Bone (GCTB) is an uncommon, locally aggressive primary bone neoplasm that may result in significant morbidity owing to its destructive growth pattern. Although intralesional curettage combined with local adjuvant therapy represents the current standard of care, this technique is associated with a relatively high incidence of local recurrence. Denosumab, a monoclonal antibody targeting RANKL (Receptor Activator of Nuclear Factor Kappa-B Ligand), has been shown to reduce tumor size, alleviate pain, and enable less extensive surgical procedures. It may also decrease the risk of recurrence and provide significant palliation in cases of metastatic or locally recurrent giant cell tumor of bone (GCTB).The series highlights the diverse clinical presentations, discusses evolving treatment strategies, and emphasizes the practical challenges faced by surgeons and oncologists in incorporating novel agents such as Denosumab into everyday practice. **Methods:** This retrospective analysis focuses on patients diagnosed with GCTB and received Denosumab at the Department of Medical Oncology, Government medical College Kozhikode between November 2022 and December 2024. Data collection included demographics, clinical presentations, diagnostic findings, treatment modalities, and follow-up outcomes. **Results:** The case series comprised various presentations, ranging from first presentation, recurrence to metastasis. 3 patients with localised disease underwent curettage with liquid nitrogen application and one patient underwent wide excision with reconstruction. Two patients who declined surgery continued on Denosumab with durable disease control. Two patients with symptomatic distant metastasis achieved symptomatic benefit and radiologic response with Denosumab therapy. **Conclusion:** This case series confirms the findings of previous studies which shows that Denosumab reduces tumor size, alleviate pain, and enables less extensive surgical procedures in GCTB. It also helps to control disease in cases of metastatic and recurrent disease. This study highlights the real word challenges faced by clinicians and highlights the need for multidisciplinary team approach in the management of GCTB.

**Keywords:** Giant cell tumor of bone- Denosumab- Bone tumor- GCTB- RANKL inhibition

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## Introduction

Giant Cell Tumour of Bone (GCTB) is a rare, locally aggressive bone neoplasm, characterized by the presence of multinucleated giant cells within a background of stromal cells. It predominantly affects the epiphyses of long bones in young adults, with a tendency for recurrence after surgical resection [1]. Despite its benign nature, GCTB has the potential for significant morbidity due to its aggressive local behaviour and risk of metastasis in rare cases. Traditional treatment options include curettage, with or without adjuvant therapies, or in some cases, limb-sparing procedures. Recently, Denosumab, a monoclonal antibody targeting RANKL, has emerged as a promising treatment option, showing efficacy in reducing tumour size, improving symptoms, and decreasing recurrence rates [2]. This retrospective case series aims to explore the role of Denosumab in managing GCTB with a

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review of literature. All patients who received Denosumab for GCTB from November 2022 to December 2024 in the Department of Medical Oncology were included in the study. The study protocol was approved by the Institutional Ethics Committee of the Government Medical College, Kozhikode (Ref. No. GMCKKD/RP 2025/IEC/72). All procedures performed in the study was in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Written informed consent was taken from the patients.

*Case Series*

C*ase 1*

A 26-year-old male presented to Orthopedics OPD in March 2023 with left shoulder pain and swelling of four months duration. On examination, his performance status was ECOG (Eastern Co-operative Oncology Group) 1. He had a hard, non-tender swelling measuring 5×4 cm over the left scapula with restricted shoulder movement. Radiography showed a lytic lesion near the glenoid process, and contrast-enhanced MRI demonstrated a well-defined lesion with cortical erosion and soft tissue extension into adjacent rotator cuff muscles (Campanacci Grade III). CT-guided trucut biopsy confirmed GCTB. The case was reviewed by our multidisciplinary tumour board (MDTB), and Denosumab therapy (120 mg subcutaneously every 4 weeks with loading doses on days 8 and 15 of the first cycle) was initiated. After six cycles, MRI showed partial response as per RECIST 1.1 (Response Evaluation Criteria in Solid Tumors) criteria, with no treatment-related adverse effects. Surgery was advised but declined by the patient, who completed 12 cycles of Denosumab. At 30 months of follow-up, he remains asymptomatic with no clinical or radiological evidence of disease progression.

*Case 2*

A 50-year-old female had a fall four weeks back and presented in a wheelchair with right leg pain and swelling to the Orthopedics OPD. On examination, her performance status was ECOG 3. She had a hard swelling measuring 10×6 cm below the right knee. Laboratory tests showed elevated ESR, raised ALP, mildly increased ALT, and low serum albumin. X-ray revealed a pathological fracture of the right proximal tibia with a lytic lesion, and MRI (April 2023) demonstrated a well-defined metaphyseal lesion with cortical destruction and displaced fracture (Campanacci Grade III). Core needle biopsy confirmed GCTB. HRCT(High resolution computed tomography) thorax excluded pulmonary metastases. Case was discussed in MDTB. She received neoadjuvant Denosumab starting from May 2023, achieving pain relief after three cycles. Post six cycles, CEMRI showed stable disease as per RECIST 1.1 criteria. The patient subsequently underwent curettage with liquid nitrogen application and proximal tibial reconstruction. At 30 months of follow-up, she remains ambulant without support, with no radiological or clinical evidence of recurrence.

*Case 3*

A 47-year-old male underwent excision of a swelling over the left middle finger in January 2021, initially reported as an aneurysmal bone cyst at an outside hospital. He was subsequently lost to follow-up. In May 2023, he presented with a one-month history of cough and recurrent hemoptysis. He had significant family history of malignancy. On examination, his performance status was ECOG 1.Chest X-ray demonstrated multiple pleural-based opacities. Contrast-enhanced CT of the chest revealed bilateral enhancing paraspinal and pleural-based soft tissue lesions with mediastinal lymphadenopathy. PET-CT confirmed FDG avid bilateral pulmonary and pleural metastases with hilar and mediastinal nodal involvement. CT-guided biopsy of the lung lesion showed spindle cells positive for CD68 and negative for cytokeratin, consistent with a mesenchymal neoplasm, suggestive of metastatic GCTB. Review of the original histopathology slides from the left middle phalanx confirmed the diagnosis of GCTB. Denosumab therapy was initiated in September 2023 after MDTB discussion, resulting in complete resolution of hemoptysis after four cycles. After six cycles, CECT showed stable disease as per RECIST 1.1 criteria. The patient has completed 18 cycles, remains asymptomatic, and continues to have stable disease at 24-month follow-up.

*Case 4*

A 24-year-old male presented in April 2022 with left ankle pain following a fall. Radiography revealed a lytic lesion in the distal tibia, and MRI confirmed a well-defined metaphyseal lesion with an intact cortex. He underwent surgical excision with bone graft reconstruction in February 2023. Histopathology showed a well-circumscribed, giant cell-rich lesion consistent with GCTB. The patient was kept under surveillance. Nine months later, he developed severe ankle pain and swelling. Repeat MRI and bone scintigraphy demonstrated a recurrent lesion with cortical breach and soft tissue extension, suggestive of Campanacci Grade III disease. On examination, ECOG performance status was 1. He had a hard swelling in the ankle measuring 6×4 cm. His case was discussed in MDTB and planned for Denosumab. He was started on Denosumab from December 2023. After six cycles, contrast-enhanced MRI showed partial response as per RECIST 1.1 criteria. However, therapy was discontinued after ten cycles due to grade 3 transaminitis.He subsequently underwent distal tibia excision with reconstruction in December 2024. At 19 months of follow-up, the patient is asymptomatic and fully ambulant, with no radiological or clinical evidence of recurrence.

*Case 5*

A 33-year-old female presented in February 2024 with pain and swelling over her right wrist of 2 months duration. On examination she was ECOG-1. There was tenderness and a restricted range of motion at the right wrist joint. X-ray revealed an expansile lytic lesion involving the

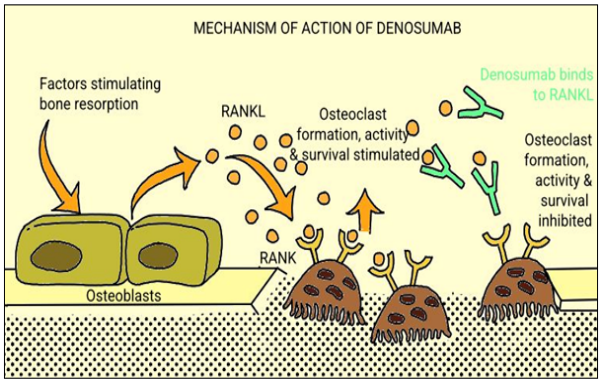


Figure 1. Denosumab is a Monoclonal Antibody that Targets and Binds to RANKL (Receptor Activator of Nuclear factor Kappa-B Ligand). By inhibiting RANKL, it prevents the activation of RANK on the surface of osteoclast precursors and mature osteoclasts, thereby reducing their formation, function, and survival.

distal radius. MRI revealed an expansile, lytic lesion in the distal third of the radius with mild joint effusion (Campanacci Grade II). FNAC confirmed the diagnosis of GCTB. She was started on neoadjuvant Denosumab protocol after MDTB discussion in April 2024 due to the tumour's proximity to the joint. After 5 cycles, CE MRI showed partial responses as per RECIST 1.1 criteria, and she underwent curettage of the lesion. Patient was then lost to follow-up. After 6 months, she developed pain at the surgical site and presented to Orthopedics out-patient department. A CE MRI scan showed recurrence of the lesion confined to the primary site. She underwent repeat curettage with liquid nitrogen application in May 2025. She is currently under follow-up with no evidence of disease in the latest MRI scan.

*Case 6*

A 37-year-old female sustained a pathological fracture of the right distal femur following a road traffic accident in September 2023. She underwent extended curettage, bone grafting, and internal fixation in October 2023. By July 2024, she developed severe knee pain and restricted joint movement. The X-ray showed progressive lateral cortical thickening and irregularity at the distal femur, raising suspicion of residual or recurrent disease. A PET-CT scan revealed mild metabolic activity in the right femoral condyle with cortical lysis. After a repeat curettage, the biopsy confirmed GCTB. She started neoadjuvant Denosumab protocol in August 2024 after MDTB discussion. After six cycles, her pain decreased but function still limited and showed a partial response according to RECIST 1.1 criteria on MRI. In February 2025, she underwent a distal femur reconstruction, curettage, and cryoablation. Histopathology post-surgery showed no malignancy or residual tumour. She is now on physiotherapy and regular follow-up.

*Case 7*

A 49-year-old male, with known psychiatric illness presented in January 2025 with pain and swelling over left knee and calf of 6 months duration. His clinical examination revealed a firm, mildly tender swelling measuring approximately 12 × 11 cm over the lateral aspect of the proximal left leg, associated with mild restriction of knee movement. Plain radiography of the left leg demonstrated a large lytic lesion with periosteal reaction involving the proximal fibula. Contrast-enhanced MRI revealed a lobulated expansile lesion arising from the proximal fibula and involving the epiphysis, metaphysis, and proximal diaphysis of the left fibula, with heterogeneous signal intensity, cortical erosion, periosteal reaction, and soft-tissue extension, consistent with Campanacci grade III disease. CT angiography showed an expansile lytic mass infiltrating adjacent muscles and encasing the anterior tibial artery. A core needle biopsy was consistent with GCTB. The patient was started on neoadjuvant Denosumab protocol after MDTB discussion. After five cycles, there was significant clinical improvement with a reduction in pain and swelling. Follow-up MRI demonstrated a partial response as per RECIST 1.1 criteria. The patient and family declined surgery and opted to continue Denosumab therapy. He has completed 8 cycles without any toxicity to date.

*Case 8*

A 34-year-old female with a history of psychiatric illness was diagnosed in 2019 with a biopsy-proven GCTB involving the sacrum. She received neoadjuvant Denosumab therapy (five cycles) followed by total sacrectomy with abdominoperineal resection in May 2019. HPR showed GCTB involving the sacrum with treatment-related changes and the patient was kept on follow-up. She remained disease-free and asymptomatic for approximately five years. In May 2024, she developed persistent low back pain. Magnetic resonance imaging (MRI) demonstrated multiple metastatic soft-tissue implants and an expansile lesion involving the right sacral ala marrow. An ill-defined soft-tissue mass with associated fluid collection was also noted inferior to the remnant sacrum, raising suspicion of local recurrence. Routine blood work up was within normal limits. A core needle biopsy confirmed recurrent GCTB. She was restarted on Denosumab therapy in mid-2024 after MDTB discussion. After 4 cycles, the patient demonstrated marked symptomatic relief and partial radiologic response on MRI, as per RECIST 1.1 criteria, with interval sclerosis and regression of the soft-tissue component. The patient continued on Denosumab and after 12 cycles there was stable disease. The Denosumab was changed to every 3 monthly and completed 18 cycles so far. No toxicity related to Denosumab to date. The patient is clinically stable and the latest imaging shows stable disease as per RECIST 1.1 criteria. The cases are summarised as Table 1.

## Discussion

Giant cell tumor of bone (GCTB) is a benign, locally aggressive tumor that primarily affects the epiphysis of long bones, especially around the knee (distal femur and proximal tibia, 44%), followed by the distal radius, proximal humerus, small bones, and sacrum. Representing

Table 1. Summary of Cases

| Sl No | Age | Sex | ECOG status | Site | Campanacci grade | Denosumab | Radiologic response by RECIST Criteria | Toxicity of Denosumab | Surgery | Follow up |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 26 | M | ECOG 1 | Left scapula | Grade 3 | Neoadjuvant 12 cycles | Partial response | No | Declined by patient | No disease progression at 30 months |
| 2 | 50 | F | ECOG 3 | Right proximal tibia | Grade 3 | -Neoadjuvant -6 cycles, | Stable disease | No | Curetting with liquid nitrogen | No disease recurrence at 30 months |
| 3 | 47 | M | ECOG 1 | Left middle finger with lung metastasis | Not applicable | -Palliative -18 cycles | Stable disease | No | No surgery | No disease progression at 24 months |
| 4 | 24 | M | ECOG 1 | Left distal tibia | Grade 3 | -Neoadjuvant -10 cycles | Partial response | Grade 3 transaminitis | distal left tibia excision and reconstruction | No disease progression at 20 months |
| 5 | 33 | F | ECOG 1 | Right distal radius | Grade 2 | -Neoadjuvant -5 cycles | Partial response | No | curetting after Denosumab. | Recurrence 6 months after curetting. Salvaged with Repeat curetting and liquid nitrogen application. No recurrence 4 months after the procedure |
| 6 | 37 | F | ECOG 2 | Right distal femur | Grade 3 | -Neoadjuvant -6 cycles | | No | distal femur makeover procedure, Bone tumour curettage, Cryoablation | Physiotherapy, under follow-up |
| 7 | 49 | M | ECOG 1 | Left proximal fibula | Grade 3 | Neoadjuvant Denosumab 5 cycles | Partial response | No | Surgery declined by patient | No disease progression. Continuing Denosumab |
| 8 | 34 | F | ECOG 1 | Sacrum post op (2029) Now with recurrence | Grade 3 | Neoadjuvant Denosumab 12 cycles | | No | | Continue Denosumab on close monitoring and surveillance |

5% of primary and 15–20% of benign bone tumors, GCTBs usually occur in adults aged 20–40 years, show slight female predominance, and are more common in Asian populations [1-6].

The precise etiology of giant cell tumor (GCT) remains uncertain, with debate over its neoplastic versus reactive nature. Giant cell tumor (GCT) of bone is primarily driven by the overexpression of RANKL by neoplastic stromal cells, which stimulates the differentiation and fusion of monocyte-derived precursors into osteoclastic giant cells. These giant cells are responsible for aggressive bone resorption through Cathepsin K and MMP-13 activity. Stromal cells also secrete osteoprotegerin, a natural RANKL inhibitor that regulates osteoclastogenesis. Somatic mutations in the H3F3A gene, found in over 90% of cases, are exclusive to stromal cells, which exhibit features of immature osteoblasts and are central to tumor development [7].

Giant cell tumor lesions typically present as soft, spongy, chocolate-brown masses with marked fragility. On gross examination, there is often cortical expansion and varying degrees of cortical disruption, although the periosteum generally remains preserved. These features aid in distinguishing GCT from other bone lesions [8]. Giant cell tumors are histologically composed of numerous multinucleated giant cells dispersed among mononuclear stromal cells. Giant cells have centrally clustered, oval nuclei with prominent nucleoli and are unevenly distributed [9]. Stromal cells may express vimentin, consistent with their mesenchymal origin, while being negative for markers of epithelial or hematopoietic lineage (e.g., cytokeratin, CD45). CD68 highlights the osteoclastic giant cells, confirming their monocytic/macrophage lineage, but is non-specific. The most specific marker for GCT is the H3F3A G34W mutation, which is present in >90% ofcases. IHC for H3F3A G34W allows highly sensitive and specific identification of neoplastic stromal cells, distinguishing GCT from other giant cell–containing lesions [10].

Patients typically report persistent localized pain, swelling, and reduced joint mobility, with symptoms often progressing over weeks to months. Pathological fractures occur in approximately 10%–30% of cases [11,12] particularly in weight-bearing bones. Tumors involving the spine or sacrum can present with neurological deficits or bowel/bladder dysfunction. In rare cases, GCTB may metastasize to the lungs.

Blood investigations including complete blood count, liver and renal function test, Serum electrolytes and Calcium,are to be done during evaluation.A plain Xray typically reveals an epiphyseal lesion with characteristic radiolucent geographic appearance with a narrow transition zone at the lesion margin, lacks a prominent sclerotic rim at the lesion margin which is called soap bubble appearance in epiphysis. CT imaging is used for assessing cortical disruption evaluating patterns of mineralization, new bone formation and overall lesion characteristics, which can assist in distinguishing between GCT and malignant conditions like osteosarcoma. A chest CT is routinely used to screen for potential lung metastases. On Magnetic resonance imaging (MRI) lesions are typically well-circumscribed, showing low signal intensity on T1-weighted and intermediate to high signal on T2-weighted images. MRI is pivotal for assessing soft tissue extension, joint involvement, and proximity to neurovascular structures in giant cell tumors supporting precise surgical planning and postoperative monitoring [8, 13]. Positron emission tomography-computed tomography (PET-CT) may help to differentiate between residual/recurrent disease from post-treatment changes and assess response to Denosumab therapy [13]. Core needle biopsy is generally preferred for confirmation of diagnosis and ruling out other malignant or benign bone tumors.In anatomically complex cases, open biopsy may be required. The Campanacci grading system for giant cell tumor of bone classifies lesions as Grade I (well-marginated intraosseous tumors with intact cortex), Grade II (larger intraosseous lesions with thinned cortex, subdivided into IIA without and IIB with pathological fracture), and Grade III (aggressive tumors with cortical breach and soft tissue extension) [14].

*Treatment*

Surgery is the primary treatment modality for GCTB.

Table 2. Denosumab in Giant Cell Tumor of Bone

| Study/Series | Design and patient number | Regimen | Key Findings |
|---|---|---|---|
| Thomas et al. [19] | Phase II, n=35 | Neoadjuvant, 3–7 doses pre-op | 86% response, >90% giant-cell reduction |
| Chawla et al. [20] | Phase II, n≈282 | Extended neoadjuvant | -No progression at 13 months.<br>- 62% patients who had surgery underwent a less morbid procedure |
| Rutkowski et al. [22] | Retrospective, 138 pts | ~11 cycles Neoadjuvant | 81% PFS at 2 yrs; better outcomes with resection |
| Tripathy SK et al [23] | Retrospective, 25 pts | 5 doses Neoadjuvant | Reduces local recurrence.<br>high function preservation |
| JCOG1610 [26] | RCT (n=106 intended) Terminated early | 5 pre-op doses Neoadjuvant | 1 yearRFS were 90.0%<br>2 year RFS :60.0% |
| Akyıldız et al., [27] | Retrospective, N=16 | Postoperative | Partial response 6%<br>Stable disease 94% |

The choice of surgical procedure is influenced by the tumor's anatomical location, Campanacci classification, and proximity to critical neurovascular or articular structures. The two main approaches are intralesional curettage and wide en bloc resection.Intralesional curettage is the standard for most Campanacci Grade I and II lesions, particularly those near joints. This approach preserves function and bone stock but carries a higher risk of recurrence. To minimize this risk, curettage is often combined with local adjuvants such as high-speed burring, phenol, cryotherapy, or polymethylmethacrylate (PMMA) cement, which also provides mechanical stability and allows early mobilization [15]. Wide resection is reserved for aggressive or recurrent tumors (typically Grade III) with cortical breach or soft tissue extension. Although this method reduces recurrence, it may compromise function, especially when joint-sacrificing procedures are involved. Reconstruction options include endoprostheses, allografts, or arthrodesis, depending on location and extent of resection [16]. Radiotherapy serves as an effective therapeutic option in cases where surgical resection is incomplete, not feasible, or would result in significant functional impairment or located in anatomically complex regions like spine and pelvis or in case of recurrent disease [17]. Commonly used dose and schedule for Radiotherapy is 50Gy in 28 fractions, 5 fraction/week over 6 weeks. Radiotherapy achieves ~80–85% 5 year local control across various settings. Larger tumor size > 8.5cm and recurrent disease are the factors associated with poor outcome [18].

Even though surgery is the standard of care,in anatomically complex or surgically morbid locations such as the spine, sacrum, or pelvis complete resection may be challenging. Denosumab acts by blocking RANKL effectively inhibit osteoclast formation and tumor activity (Figure 1). Denosumab is evolved as a valuable neoadjuvant therapy in this context by inducing tumor regression and facilitating more conservative surgical approaches.The pivotal phase II trial by Thomas et al. demonstrated the initial efficacy of Denosumab in 37 patients with recurrent or unresectable GCTB. Denosumab led to the near-complete elimination of giant cells in 86% of patients, with radiographic evidence of bone formation and significant symptomatic improvement [19]. These promising findings prompted a larger phase II study by Chawla et al, involving 282 patients. In this trial, 96% of patients achieved at least a 90% reduction in osteoclast-like giant cells. Among the cohort where surgery was initially planned, 74% experienced reduced surgical morbidity, including conversion from planned en bloc resections to curettage or limb-sparing procedures [20]. Similarly, another study by Beresford-Cleary et al noted the use of Denosumab in spine GCT in acute setting showed significant reduction in pain and size of tumor enabling less invasive surgeries [21]. The European multicenter experience of 138 patients with locally advanced GCTB treated with Denosumab reported that neoadjuvant Denosumab facilitated wide resections or curettage. Two-year PFS was 81%; significant recurrence reduction with wide resection (93% vs 55%) [22]. A retrospective study from India recruited 25 high-risk Campanacci II/III patients who received five neoadjuvant doses prior to surgery (curettage or prosthesis). Only 1 recurrence at 40-month follow-up; functional scores were excellent [23]. In Another study from India 44 GCTB patients were treated with 5–7 preoperative Denosumab cycles. Surgery intentions were met in 95%; 2 year LRFS was 76%, with better control after resection vs curettage (94% vs 64% [24]. A Russian study demonstrated that neoadjuvant Denosumab reduced the risk of progression compared to surgery alone [25]. The JCOG1610 phase 3 trial which tried to confirm the superiority of preoperative Denosumab to curettage with adjuvant local therapy was terminated early due to poor patient enrollment and results did not show any benefit in recurrence free survival without large post-op bone defect [26].

There are limited data for the exclusive adjuvant use of Denosumab after curettage. A study by Akyıldız et al. used a post operative Denosumab in 18 patients and reported stable disease in 94% of the patients [27]. Most guidelines recommend individualized consideration for adjuvant Denosumab, particularly in patients with high-risk features for recurrence or those unfit for repeat surgery. Trials of Denosumab in GCTB are summarized as Table 2.

However, concerns regarding local recurrence after Denosumab have emerged and studies report varying rate of recurrence. Errani et al. compared patients who underwent curettage with and without prior Denosumab and found significantly higher recurrence in the Denosumab group (60% vs. 16%). This increased risk is thought to be related to altered tumor histology and masked residual disease due to new bone formation [28]. A multicenter study observed a 35% local recurrence rate after curettage in patients treated with Denosumab as a neoadjuvant therapy [29]. Another systematic review encompassing seven studies found recurrence rates ranging from 20% to 100% in the neoadjuvant Denosumab group, compared to 0% to 50% in the curettage-alone group [30]. A meta-analysis of eight studies indicated that preoperative Denosumab increases the risk of local recurrence after surgery in patients with GCTB. The analysis revealed a higher risk of local recurrence in the Denosumab group compared to the curettage-alone group, with an odds ratio of 2.29 [31]. The increased risk of local recurrence following Denosumab therapy underscores the importance of considering additional treatment strategies and close postoperative monitoring to improve long-term outcomes for patients with GCTB.

Bisphosphonates inhibit osteoclast-mediated bone resorption by binding to bone surfaces and disrupting osteoclast function. This leads to osteoclast apoptosis, reduced bone turnover, preserved bone density which has demonstrated in preclinical trials to control the growth of GCTB.In one randomized trial involving 30 patients with extremity GCTB, the use of neoadjuvant zoledronic acid resulted in no local recurrences at a median follow-up of 28 months [32]. Studies exploring use of Bisphosphonate-loaded polymethylmethacrylate (PMMA) cement, which allows for local drug delivery after curettage has shownto reduce local recurrence (6%) with minimal adverse

events [33]. A recent meta-analysis of 181 patients enrolled in 8 clinical studies from 2008-2020 confirmed that preoperative/postoperative Bisphosphonate reduces recurrence rates [34]. Bisphosphonate can be used as an alternative option for patients with GCTB who cannot afford Denosumab especially from the low middle income countries like India but the long-term toxicities like osteonecrosis of jaw and renal toxicity should be kept in mind. The PDL1 expression is around 28% and Immunotherapy may be an option for unresectable or Metastatic GCTB progressing on Denosumab [35].

Tumors of the spine, sacrum, or pelvis have higher recurrence due to surgical complexity. Recurrence risk increases with higher Campanacci grade. Wide resection (<10% recurrence) is superior to curettage (20–50%), and adjuvants like phenol, PMMA, or cryotherapy reduce recurrence. Neoadjuvant Denosumab shrinks tumors but may obscure margins, increasing recurrence if resection is incomplete. Pulmonary metastasis (1–4%) and malignant transformation (<2%) are rare, emphasizing close follow-up [13].

The case series comprised various presentations, ranging from first presentation, recurrence to metastasis. 3 patients with localised disease underwent curettage with liquid nitrogen application and one patient underwent wide excision with reconstruction. Two patients who declined surgery continued on Denosumab with durable disease control. Two patients with symptomatic distant Metastasis achieved symptomatic benefit and radiologic response with Denosumab therapy. One patient developed persistent transaminitis and required to stop Denosumab.

In conclusion, the neoadjuvant Denosumab helped in performing less morbid surgery in our patients. Patients who were unwilling for surgery had excellent clinical and radiologic responses and durable disease control. The use of Denosumab in metastatic/recurrent GCTB lead toclinical and radiologic response and prolonged disease control. Accessibility to Denosumab and Curetting with liquid Nitrogen is limited to high end centres in the LMIC setting. Our study shows the real-world challenges faced by clinicians in managing GCTB.

*Declarations*

*Clinical trial registration*

Not applicable.

*Conflicts of interest/ Competing interests*

Authors declare that they have no conflicts of interest

*Availability of data and material*

The data sets used during the current study are available from the corresponding authors per reasonable request.

*Code availability*

Authors' contributions: All authors contributed equally to the data collection and preparation of manuscript.

*Ethics approval*

This study was approved by the Institutional Ethics Committee of Government Medical College Kozhikode(Ref. No. GMCKKD/RP 2025/IEC/72).

*Consent to participate*

Written informed consent was obtained from all participants, and the trial was conducted in accordance with the Declaration of Helsinki.

*Consent for publication*

Written informed consent was obtained from all participants, and the trial was conducted in accordance with the Declaration of Helsinki.

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*Declaration on generative AI and AI-assisted technologies in the writing process*

Not applicable.

*Originality Declaration for Figures*

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