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Case Report

Primary malignant giant cell tumor (PMGCT): Diagnosis and management challenges in low resource settings

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Abstract

Bone primary malignant giant cell tumor (PMGCT) cases are extremely rare, and the optimal management remains unclear. This case report details the diagnosis and successful management of PMGCT in a 45-year-old female presenting with left knee pain, swelling, and restricted movement for one year. Accompanying weight loss and loss of appetite led the patient to seek tertiary care after unsuccessful prior treatment. Imaging, including X-ray and magnetic resonance imaging (MRI), revealed a tumor measuring 7.9 × 7.7 × 6.6 cm, and histopathological examination using fine needle aspiration cytology confirmed the diagnosis of PMGCT. A multidisciplinary approach was taken, involving orthopedic surgery to remove the tumor successfully, and physiotherapy for postoperative care. The patient underwent tumor excision and curettage under spinal and epidural anesthesia, followed by a week of bed rest, and then physiotherapy was started to aid in limb mobilization. Postoperative care involved blood transfusions, femoral artery stenting, continued physiotherapy and adjuvant radiotherapy, initiated two weeks post-surgery, with a total dose of 50 Gy delivered in 25 sessions to reduce the risk of recurrence. Initial monthly follow-ups, later transitioning to quarterly, showed improved joint mobility and function, with no recurrence at the 9-month follow-up. This case highlights the importance of early diagnosis and a multidisciplinary approach to managing PMGCT. Collaboration across specialties contributed to the positive outcome, even in a resource-limited setting. Long-term monitoring remains essential to detect recurrence, and further research is needed to refine treatment strategies for malignant GCTs.

Keywords: Giant cell tumor, primary malignant giant cell tumor, pathological fracture, accidental diagnosis, multidisciplinary approach

Introduction

Giant cell tumors (GCTs) of the bone represent a clinically significant entity due to their locally aggressive behavior and potential for recurrence [1]. While these tumors are typically benign, a small percentage can transform into malignant GCTs, which have the capacity for metastasis and more aggressive clinical behavior. Malignant GCTs are extremely rare and are classified into two types: primary malignant GCT (PMGCT) and secondary malignant GCT (SMGCT) [2]. PMGCT arises when a high-grade sarcoma develops alongside a benign GCT, whereas SMGCT occurs in previously treated GCT sites, often after radiation or recurrence [3]. PMGCTs are highly rare,

Received: July 1, 2024 - Accepted: November 10, 2024 - Published online: January 8, 2025

occurring in only 1–2% of all reported GCT cases, but they tend to have a comparatively better prognosis than SMGCTs [4]. The peak incidence of GCTs occurs between the 3rd and 5th decades of life, with a slightly higher occurrence in females, with a female-to-male ratio of 1:0.8 [5,6].

GCTs typically arise in the epimetaphysis of long bones, particularly around the knee joint. The distal end of the femur is one of the most common locations for GCTs [7]. When GCTs occur in this region, they can cause significant morbidity, primarily due to their proximity to the knee joint [8]. This location increases the risk of pathologic fractures, particularly intra-articular fractures, which can lead to joint instability, impaired mobility, and chronic pain. The neoplastic stromal mononuclear cells, along with multinucleated giant cells and mononuclear histiocytic cells, drive the pathological process [9,10]. It is believed that the stromal cells express receptor activator of nuclear factor kappa-B ligand (RANKL), which recruits the osteoclast-like giant cells responsible for the characteristic osteolysis [11]. Cathepsin K, a protease unique to these giant cells, is thought to be a key factor in the bone destruction seen in GCTs [12]. As a result, patients with GCT of the distal femur are at high risk of functional impairment, disability, and decreased quality of life due to the involvement of the adjacent knee joint.

Management of GCTs remains a challenge, particularly due to their location and potential for recurrence [13]. Various treatment modalities have been employed, including surgical excision, curettage, arterial embolization, cryotherapy, and radiation. In the case of GCTs of the distal femur, surgical intervention is often necessary to prevent joint damage and maintain limb function. However, there remains a risk of recurrence and complications, such as knee joint instability or the need for subsequent joint replacement surgery. The efficacy of these interventions has been widely documented in the context of long-bone lesions [14].

This case report presents the management of a PMGCT in a 45-year-old female. The tumor was located in the distal end of the left femur, with a tumor size of 7.9 × 7.7 × 6.6 cm, which was managed by excision and curettage under spinal and epidural anesthesia. This case is noteworthy not only because of the malignant nature of the tumor but also due to its location in the distal femur, where its proximity to the knee joint posed a significant risk for post-surgical complications and functional impairment. The aim of this study was to address current knowledge gaps by discussing the decision-making process and treatment challenges associated with PMGCTs of the distal femur, particularly in terms of preserving joint function and preventing recurrence.

Case

A 45-year-old female presented to the Orthopedic Department of Acharya Vinoba Bhave Rural Hospital in Wardha, Maharashtra, India, with a one-year history of left knee pain and swelling, accompanied by restricted movement. The patient had a history of two falls: the first one year ago and another 15 days before presentation. Over the past month, the patient experienced significant weight loss, loss of appetite, and an inability to walk. The patient had no history of loss of consciousness, bleeding, chronic illnesses, or previous surgeries. Oral medications prescribed by a private practitioner provided no relief, prompting the patient to seek further management.

On physical examination, the patient was afebrile, with a pulse rate of 82 beats/min and blood pressure of 110/80 mmHg. The patient exhibited pallor without other systemic signs (such as icterus, clubbing, cyanosis, pedal edema or lymphadenopathy). There was diffuse swelling over the left knee, which was warm and tender and had a restricted range of motion (ROM) limited to 80 degrees. Active ankle movements were present, and distal circulation was intact.

Blood investigations revealed anemia, with a hemoglobin level of 8.7%, decreased mean corpuscular volume (MCV) of 59.6 fL, and mean corpuscular hemoglobin (MCH) of 18.6 pg. Other notable findings included a reduced hematocrit of 27.9%, elevated red blood cell distribution width (RDW) of 19.2%, and a peripheral smear showing microcytic, hypochromic red cells with anisopoikilocytosis.

Imaging studies were pivotal in establishing the diagnosis. An X-ray of the left knee showed cortical destruction of the lateral condyle of the femur (**Figure 1A**). Further evaluation with contrast-enhanced magnetic resonance imaging (MRI) revealed an altered signal intensity lesion measuring 7.9 × 7.7 × 6.6 cm, with soft tissue involvement and edematous changes adjacent to the lateral femoral condyle (**Figure 1B**). The lesion's appearance on MRI—hypointense on T1-

weighted and heterogeneously hyperintense on T2-weighted images—suggested a diagnosis of GCT or chondrosarcoma. To confirm the diagnosis, a fine needle aspiration cytology (FNAC) of the distal femur was performed, followed by a histopathological examination of the tumor and surrounding soft tissue. Histopathology confirmed the diagnosis of PMGCT, showing vascular and capsular invasion by malignant epithelial cells (**Figure 1C**).

Surgical excision and curettage of the PMGCT were performed under spinal and epidural anesthesia. A 15 cm incision was made on the lateral thigh to expose the distal femur, where the tumor involved the anterior, medial, and posterior cortex. The tumor mass was completely excised, and the cavity was filled with bone cement after thorough cleaning with hydrogen peroxide, betadine, and normal saline. Hemostasis was achieved by cauterization, and the wound was closed with a drain in place. Postoperative imaging confirmed satisfactory resection (**Figures 1D** and **1E**).

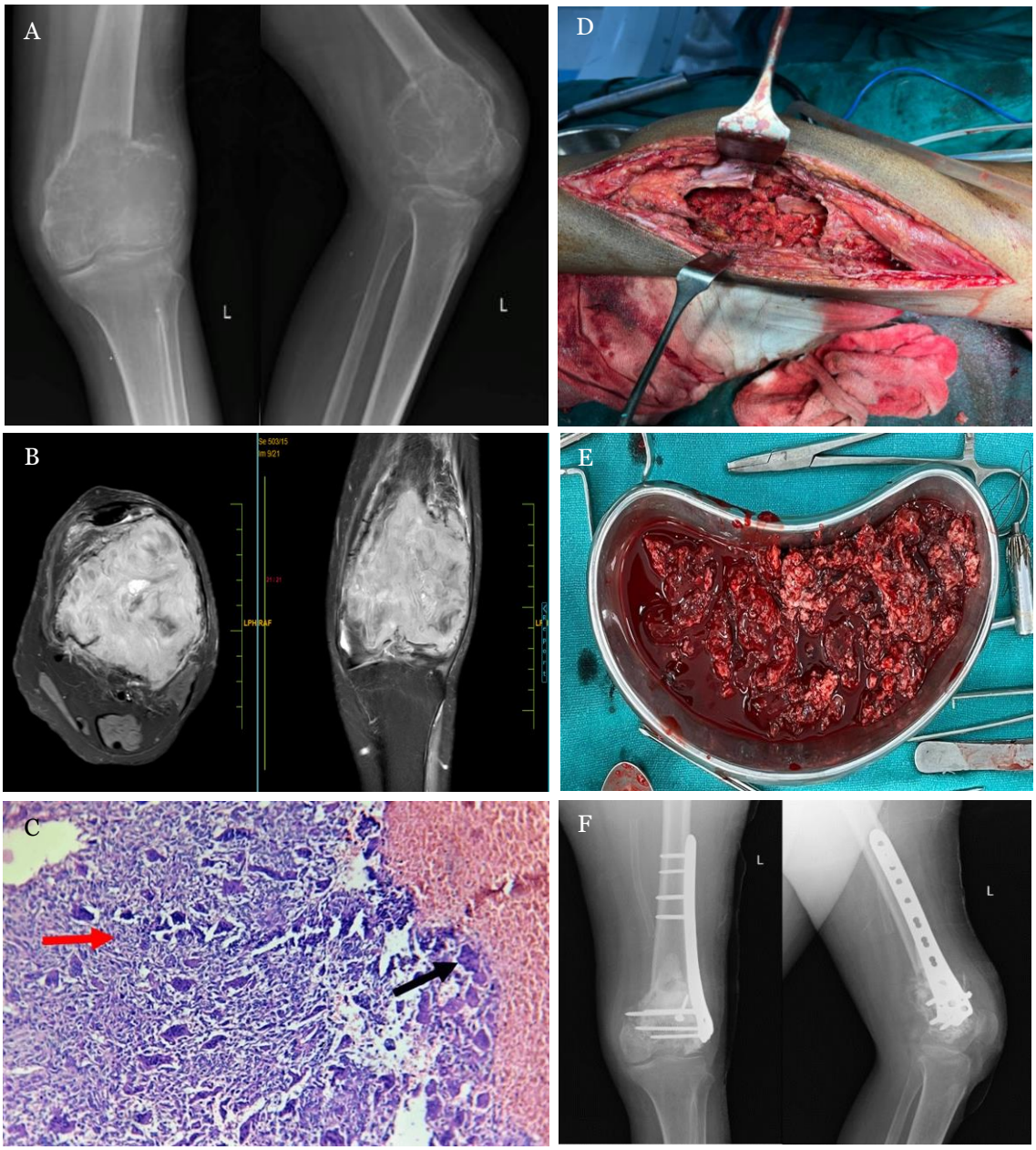

Figure 1. (A) Preoperative X-ray anteroposterior and lateral view of the left knee. (B) Preoperative contrast-enhanced magnetic resonance imaging (CEMRI). (C) Histopathological examination showed infiltration of malignant epithelial cells (the black arrow showed the presence of multinucleate osteoclast-like giant cells, and the red arrow showed the presence of round to spindle-shaped mononuclear cells). (D) Intraoperative view of the tumor before curettage. (E) The excised tumor masses. (F) Postoperative X-ray anteroposterior and lateral view of the left knee.

Postoperatively, the patient required four rounds of blood transfusion (approximately 1 L of blood) to address the anemia. The patient also underwent stenting of the left superficial femoral artery under local anesthesia, which was well-tolerated. Postoperative care included analgesics, antibiotics, and physiotherapy to improve the knee's range of motion. A long knee brace was used, and non-weight-bearing mobilization was initiated with the help of a walker. Suture removal was done on the 12th postoperative day with no complications.

Follow-up X-rays showed a satisfactory outcome, and the patient reported improved mobility during her follow-up visit one month after surgery (**Figure 1F**). The patient was advised to continue physiotherapy and oral medications, including calcium and vitamin C supplements. Radiotherapy was also administered post-surgery to reduce the risk of recurrence. A targeted protocol was developed by the oncology team, focusing on the affected area around the knee and femoral region. The patient received external beam radiotherapy (EBRT) in fractions of 2 Gy per session, delivered five days a week, for a total of 25 sessions. This approach brought the cumulative dose to 50 Gy, a standard regimen shown to be effective in preventing local recurrence. Each session lasted approximately 15 minutes, with careful attention to patient positioning and shielding of surrounding tissues to minimize adverse effects. The patient did not report any complications and tolerated the treatment well. Upon completion, the follow-up MRI showed no signs of local recurrence or new growth, and the patient continued to report steady improvement in mobility and decreased pain, marking a successful outcome from both the surgical and radiotherapy interventions.

This case highlights the challenges in diagnosing and managing PMGCT of the distal femur, particularly due to the proximity of the knee joint, which posed a significant risk of joint instability and post-surgical complications. The successful surgical intervention, combined with a multi-disciplinary approach involving radiotherapy and physiotherapy, contributed to the patient's positive outcome.

Discussion

Benign GCTs, which account for about 5% of all bone neoplasms, are typically non-metastatic, but a small percentage can transform into malignant GCTs, which have the capacity for metastasis and show more aggressive clinical behavior, called malignant GCTs (MGCT) [15]. These are extremely rare and classified into two types: primary malignant GCT (PMGCT), and secondary malignant GCT (SMGCT). PMGCTs are a rare and aggressive subtype, occurring in 1–2% of GCT cases [16]. This rarity makes PMGCTs a particularly challenging condition to diagnose and manage effectively. In our case, the patient presented with a PMGCT in the distal femur, which was successfully managed with surgical excision and radiotherapy, improving the quality of life. Postoperatively, the patient showed significant improvements in quality of life and functional outcomes. Initially, the patient reported considerable pain, with a preoperative visual analog scale (VAS) score of 8/10, which decreased to 3/10 at one-month follow-up. The knee mobility also improved notably: preoperatively, the range of motion was limited to 80 degrees due to pain and swelling, and following surgery and structured physiotherapy, the range of motion increased to 90 degrees, enhancing independence in daily activities. Follow-up imaging showed no residual tumor or recurrence, indicating a favorable prognosis. The combination of surgical resection and radiotherapy, often linked to reduced recurrence rates in PMGCT cases [17], contributed to this patient's improved prognosis. Consequently, the projected life expectancy aligns with reported outcomes in similar case series [18], where adjuvant radiotherapy and bone cement filling effectively lower recurrence risks, supporting better overall survival rates. This case highlights the importance of early detection, as older age and delayed diagnosis are significant prognostic factors for worse outcomes [19]. A study demonstrated that older patients have more advanced disease at diagnosis and a 41% increase in the risk of mortality for every five years of delayed detection [20]. Moreover, patients with distant metastases at diagnosis are 5.2 times more likely to die compared to those whose tumors are confined to the bone [15].

The prognosis of MGCT, especially SMGCT, is poor [21-24]. A study noted higher mortality rates in SMGCT patients, despite surgical and chemotherapeutic interventions [25]. MGCT patients had a five-year survival rate of only 50% even after surgery and chemotherapy, emphasizing the aggressive nature of these tumors [15]. In this case, the use of radiotherapy

adjunct with surgery led to a positive short-term outcome for the patient, with a 9-month follow-up showing no signs of recurrence or complications. Interestingly, a study reported a more favorable prognosis for some MGCT patients, with a mean survival duration of 11 years and 11 months and a five-year relative survival rate of 84.2% [20]. Another study noted a lower, yet significant, mortality rate of 16% and a five-year survival rate of 87%, which may suggest that some MGCTs exhibit low-grade malignancy [19]. These diverse prognosis data are mainly due to the tumor's rarity and brief follow-up periods. In our case, we were able to monitor the patient over a 9-month period, which demonstrated a favorable outcome, though longer follow-up would be necessary to assess long-term recurrence.

This case is unique not only due to the rarity of PMGCT but also because it was managed successfully in a resource-limited setting in rural central India. The ability to provide effective treatment, including surgical excision, blood transfusions, and postoperative care with limited resources, demonstrates the adaptability of treatment protocols for managing complex bone tumors like MGCT in such settings. Furthermore, the case illustrates the potential for improved outcomes with a multidisciplinary approach, even in a rural environment.

One of the limitations of this case is that it is only nine months old, which restricts our ability to comment on long-term recurrence or overall survival. Future follow-up of similar cases would be crucial in understanding the long-term impact of the treatment strategies employed. The lack of advanced resources for chemotherapy also limited the therapeutic options available to the patient, which could have implications for recurrence risk. However, the case still contributes valuable insights into the management of PMGCT in resource-constrained environments.

Conclusion

This case demonstrates the importance of early diagnosis and a multidisciplinary approach in managing PMGCT cases. The favorable one-year outcome, indicated by improved joint function, absence of recurrence, and enhanced quality of life, suggests that surgery combined with radiotherapy can be effective even in resource-limited settings. Further research and long-term follow-up are needed to understand better the prognosis of PMGCT and the optimal management strategies, particularly in under-resourced areas.

Ethics approval

Written informed consent has been provided by the patient for publication of this case report.

Acknowledgments

Authors have no acknowledgments to be stated.

Competing interests

All the authors declare that there are no conflicts of interest.

Funding

This study received no external funding.

Underlying data

Derived data supporting the findings of this study are available from the corresponding author on request.

Declaration of artificial intelligence use

We hereby confirm that no artificial intelligence (AI) tools or methodologies were utilized at any stage of this study, including during data collection, analysis, visualization, or manuscript preparation. All work presented in this study was conducted manually by the authors without the assistance of AI-based tools or systems.

How to cite

Prasad R, Shukla S, Acharya S, *et al*. Primary malignant giant cell tumor (PMGCT): Diagnosis and management challenges in low resource settings. Narra J 2025; 5 (1): e1088 - http://doi.org/10.52225/narra.v5i1.1088

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