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Malignant transformation of giant cell tumor of bone with pulmonary metastasis: Case report

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Abstract
Background: Giant cell tumor of bone (GCTB) is a benign but locally aggressive tumor that usually affects the epiphysis of long bones in young adults. Although most cases are effectively treated with intralesional curettage and local adjuvants, malignant transformation is a rare but devastating complication. Secondary transformation is typically associated with prior radiotherapy, while post-surgical sarcomatous change without radiation is exceptionally uncommon.
Case Presentation: We present the case of a 40-year-old male with progressive left knee pain and swelling. Imaging demonstrated a lytic lesion in the distal femoral condyle, and histopathology confirmed a benign GCTB. The patient was treated with curettage and defect filling using polymethylmethacrylate (PMMA) cement. Six years later, he experienced the onset of progressively worsening knee pain. Imaging studies showed suspicion of a malignant lesion. Biopsy confirmed a high-grade osteosarcoma arising in the previously treated site, consistent with secondary malignant transformation of GCTB. After multidisciplinary discussion, the patient received neoadjuvant chemotherapy, followed by *en bloc* resection of the distal femur and total knee arthroplasty with a tumoral prothesis. Histology confirmed a grade III osteosarcoma with clear margins, and adjuvant chemotherapy was completed. Two years later, routine surveillance detected a solitary pulmonary metastasis, which was biopsy-confirmed and managed with palliative radiotherapy. The patient remains under close oncological follow-up.
Conclusion: This case highlights the rare occurrence of a secondary high-grade sarcoma arising after surgical treatment of a benign GCTB without radiotherapy. It emphasizes the importance of long-term surveillance and the value of multidisciplinary management in optimizing outcomes in these aggressive and complex cases.

Keywords: Giant cell tumor of bone, bone tumours, osteosarcoma, malignant transformation, pulmonary metastasis

Introduction
Giant cell tumor of bone (GCTB) is a locally aggressive but benign neoplasm that accounts for approximately 4–5% of all primary bone tumors [1]. It characteristically affects the epiphyseal-metaphyseal regions of long bones in young adults [1].
Although benign, GCTB exhibits unpredictable behavior: local recurrence is common, pulmonary metastases occur in a small fraction of cases (~2-7%), and very rarely, the tumor may undergo malignant transformation [2]. Malignant transformation can be classified into primary malignant GCTB, which presents as high-grade sarcomatous areas coexisting with conventional GCTB at initial diagnosis, and secondary malignant GCTB, which develops after a latency period following treatment of a conventional GCTB [1, 2, 3]. The incidence of malignant transformation in GCTB is low—most studies report rates around 1-4% [4].
When malignancy occurs, it is typically high-grade, often of osteosarcoma, undifferentiated pleomorphic sarcoma, or fibrosarcomatous type [3]. The prognosis is markedly worse than for benign GCTB, especially in the presence of distant metastasis (for example, to the lungs), which often signals systemic disease and limits therapeutic options [1, 3].
Herein, we report a case of secondary malignant transformation occurring five years after resection of a benign GCTB, with development of a high-grade sarcoma at the same site and associated pulmonary metastases, underscoring the importance of long-term surveillance and the challenge in management once malignant transformation has occurred.

Materials and Methods

Clinical records of the patient were collected and analyzed.

Case Report

A 40-year-old male presented in 2017 with several months of progressive left knee pain and swelling. Physical examination revealed localized tenderness over the lateral distal femur, without neurovascular compromise. Radiographs and CT scan demonstrated a lytic, expansile lesion in the lateral femoral condyle, extending to the subchondral region, with well-defined margins and no periosteal reaction (Fig.1). MRI confirmed an epiphyseal lesion with cortical thinning but no extraosseous extension. These findings were suggestive of a giant cell tumor of bone (GCTB).

The patient underwent intralesional surgery with aggressive curettage and meticulous removal of residual tumor tissue from the cavity walls, followed by filling the defect with polymethylmethacrylate (PMMA) cement to provide immediate structural stability. Histopathology confirmed a benign GCTB, characterized by numerous osteoclast-like giant cells among mononuclear stromal cells, with no atypia or sarcomatous features. Postoperative recovery was uneventful; the patient returned to full weight-bearing and resumed his daily activities at pre-surgical levels. Clinical and radiological follow-up over six years revealed no evidence of recurrence.

At age 46, the patient began experiencing progressive left knee pain. Examination revealed localized tenderness and restricted range of motion. Imaging demonstrated a destructive lesion with cortical breakthrough adjacent to the cemented cavity, and MRI showed an infiltrative mass with soft-tissue extension (Fig.2). Chest CT was initially negative for metastases. Open biopsy revealed spindle-cell proliferation with nuclear atypia, abundant mitotic figures, and osteoid production, consistent with a high-grade (grade III) osteosarcoma arising in the previously treated GCTB, confirming secondary malignant transformation.

Following multidisciplinary discussion, the patient received neoadjuvant chemotherapy with high-dose methotrexate, doxorubicin, and cisplatin. He then underwent wide en bloc resection of the distal femur, followed by reconstruction with a total knee arthroplasty using a tumoral megaprosthesis (Fig.3). Histopathological examination confirmed a high-grade sarcoma with clear surgical margins. Pathological staging was T2N0M0.

The patient completed adjuvant chemotherapy with the same regimen. Routine surveillance was performed. Two years later, in May 2025 (age 48), chest CT revealed a new solitary pulmonary nodule, suspect for malignancy. Biopsy was performed and confirmed a metastatic lesion. Multidisciplinary review recommended palliative radiotherapy for local control, with systemic management under ongoing consideration.

The patient continues under close oncological follow-up, with no new lesions identified to date.

Figure format

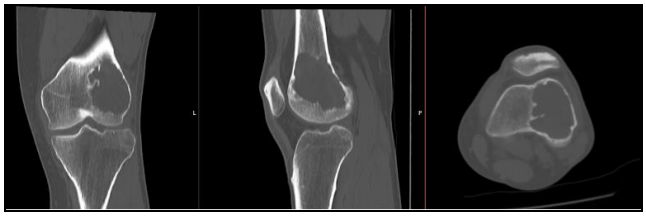

Fig 1: Pre-operative CT-scan

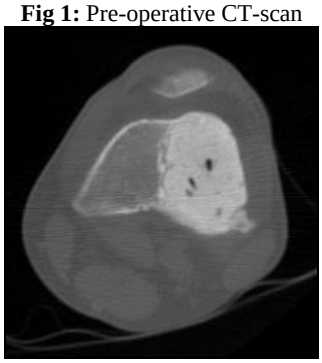

Fig 2: Malignant GCTB

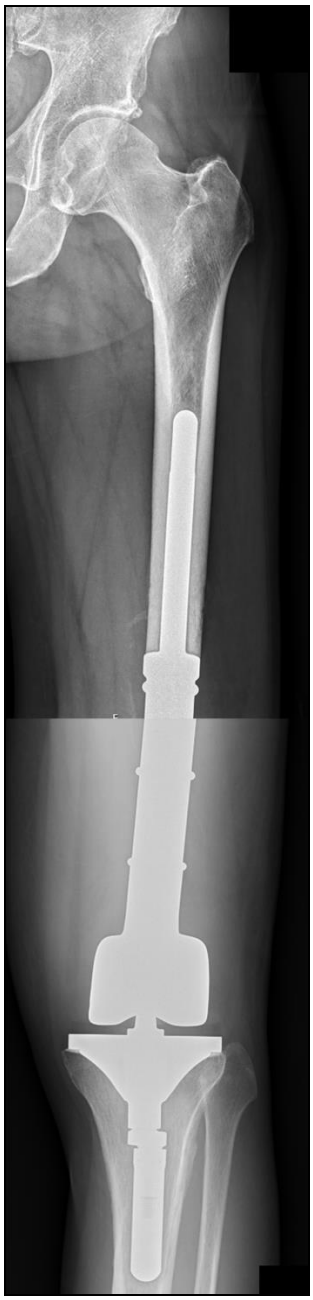

Fig 3: Knee reconstruction with a tumoral prothesis

Discussion

Giant cell tumor of bone (GCTB) is a generally benign, but locally aggressive, neoplasm. It accounts for approximately 6% of all primary bone tumors.

Although curettage with adjuvant local therapy and cement filling is standard management, malignant transformation is a rare but well-documented complication, occurring in less than 1% of cases, typically years after initial treatment [5]. Secondary malignancy is most often associated with prior radiotherapy, but spontaneous or post-surgical sarcomatous transformation has also been reported, as in the present case [1].

Our patient underwent intralesional curettage with PMMA cement augmentation, without any adjuvant radiotherapy. He remained disease-free for six years, consistent with typical GCTB behavior, before developing progressive pain and radiographic evidence of an infiltrative lesion. Histopathology confirmed a high-grade (grade III) osteosarcoma arising in the previously treated site, representing a rare case of secondary malignant GCTB. The interval of six years is within the range reported in the literature for post-surgical sarcomatous transformation, which may vary from 2 to more than 15 years [1].

The pathogenesis of secondary sarcomatous transformation after intralesional surgery is not fully understood. Several hypotheses have been proposed, including genetic instability in stromal cells, chronic local irritation from PMMA cement, and the proliferative stimulus induced by bone remodeling [1]. Although cement is widely used for structural support and local tumor control, its role as a potential contributor to sarcomatous transformation remains speculative [6].

Management of secondary high-grade sarcomas arising from GCTB follows standard sarcoma protocols, including neoadjuvant chemotherapy, wide resection, and reconstruction with prosthetic replacement when necessary [7]. In this patient, multidisciplinary treatment with neoadjuvant MAP chemotherapy, wide distal femoral resection, and reconstruction with a total knee arthroplasty tumor prosthesis achieved local control, while adjuvant therapy was completed per protocol. Pulmonary metastasis identified two years postoperatively highlights the aggressive nature of secondary sarcomas and underscores the need for continued close surveillance [8].

This case emphasizes several important clinical points. First, patients with GCTB treated surgically, even without radiotherapy, require long-term follow-up due to the rare but serious risk of malignant transformation. Second, any new pain, functional limitation, or radiographic change at the prior tumor site warrants prompt imaging and biopsy to rule out malignancy. Finally, multidisciplinary management, including orthopedic oncology, medical oncology, radiology, and pathology, is essential for optimal outcomes in these rare and complex cases.

Conclusion

In conclusion, secondary high-grade sarcoma arising from a previously treated GCTB is extremely rare but carries significant morbidity. Early recognition, appropriate imaging, biopsy confirmation, and aggressive multimodal management are critical for improving patient outcomes.

Acknowledgments

The authors have no conflict of interest to declare.

Conflict of Interest

Not available

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Not available

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