Primary malignant giant cell tumour of the proximal tibia: a case report

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Abstract

Primary malignant giant cell tumour of bone is extremely rare and very few examples exist in the literature. We report a case of a 37-year-old man with a primary malignant giant cell tumour of the proximal tibia. He was HIV positive on anti-retroviral treatment and had no history of radiotherapy or prior surgery. Radiographic staging included an MRI scan that clearly defined two distinctly different, juxtaposed tumours. These two tumours were histologically confirmed as a giant cell tumour with no evidence of malignancy and a conventional osteosarcoma.

Keywords: giant cell tumour; primary malignant transformation; osteosarcoma; magnetic resonance imaging
histologically be typified as fibrosarcoma, osteosarcoma or pleomorphic undifferentiated sarcoma (previously known as malignant fibrous histiocytoma) [5, 15].

We report a case of a 37-year-old male who was diagnosed with histologically benign GCT of bone, juxtaposed with a high-grade conventional osteosarcoma. This case report highlights the importance of pre-biopsy Magnetic Resonance Imaging (MRI) in determining the ideal biopsy site in order to obtain a representative histological sample.

**Case report**

A 37-year-old man was referred to our tertiary level tumour unit with a three-year history of a slow growing, painful mass in the region of the left proximal tibia. The histological diagnosis of a giant cell tumour was made at his base hospital prior to being referred to our institution.

The initial presentation to his base hospital was prompted by a painful mass of the left proximal tibia that was slowly enlarging over the preceding two years. An incisional biopsy was done at the antero-lateral aspect of the proximal tibia. The histological diagnosis of giant cell tumour of bone was made. It is unclear why the patient did not seek any further treatment at that stage and no attempt at resection or radiation therapy was made. Over the ensuing 10 months, the lesion continued to progress, prompting return to his local hospital and subsequent referral to our orthopaedic tumour unit.

At presentation to our institution, the patient had a large, painful proximal tibial tumour and an 80-degree knee fixed flexion contracture (Figure 1). Weight bearing was not possible due to the severe knee flexion contracture. The patient was admitted for local and systemic staging in preparation for repeat biopsy and definitive intervention.

The patient was known to be HIV positive on Highly Active Anti-retroviral Therapy (HAART) and systemic staging revealed a CD4 count of 301 cells/ml. No other comorbidities were identified. Computerized Tomography (CT) scan of the chest and abdomen did not identify any metastatic lesions, while a bone scintigraphy scan only displayed increased activity of the left proximal tibia.

Local staging included radiographs and an MRI scan. The radiographs showed a locally aggressive, geographic lytic lesion located in the proximal tibia with thinning and expansion of the cortex (Figure 2). MRI scans revealed two juxtaposed, distinctly different lesions, with the proximal lesion exhibiting classic GCT features of heterogenous intermediate T2 signal for the solid portion of the tumour and high T2 signal cystic areas (Figure 3, Arrow 1). The distal lesion however, was more solid in nature and appeared predominantly hypo-intense in both the T1 and T2 sequences (Figure 3, Arrow 2).

**Figure 2** AP and lateral radiographs showing a large, geographic lytic lesion of the proximal tibia with cortical thinning, expansion and destruction.

**Figure 3** MRI scan with features of a giant cell tumour at arrow 1 and an osteosarcoma at arrow 2.

Biopsy was guided by the MRI findings and consisted of an incisional biopsy of both the proximal and distal aspects of the lesion. Histological evaluation of the proximal section revealed a classic GCT with no malignant features (Figure 4), while the distal extent of the tumour was characterized as conventional high-grade osteosarcoma (Figure 5).
to the local extent of the tumour and the associated knee flexion contracture, neo-adjuvant chemotherapy and limb salvage was not considered. An above knee amputation was performed with subsequent adjuvant chemotherapy and at one year follow-up the patient had no local recurrence or systemic disease.

![Figure 4 Histological specimen showing benign giant cell tumour.](image)

![Figure 5 Histological specimen showing conventional osteosarcoma.](image)

**Discussion**

The World Health Organization (WHO) classifies giant cell tumours of bone as benign lesions that are locally aggressive and potentially malignant [16]. These tumours are typically located in the juxta-epiphyseal region of long bones in post-pubertal adolescents and young adults, with the proximal tibia and distal femur being the most commonly affected sites [1, 5, 8, 17].

Histologically, two cell types characterize GCTs, mononuclear stromal cells and multinucleated osteoclast-like giant cells [1, 8]. The mononuclear stromal cell component is comprised of two distinct cell lines; mononuclear round cells (minor component) ad mononuclear spindle shaped cells (major component) [8, 18]. The minor component cells express monocyte-macrophage markers and represent the non-neoplastic element [8, 10, 18, 19]. The major component cell line is thought to arise through mesenchymal cell neoplasia or metaplasia and represents the neoplastic component [8, 10, 18]. These cells secrete various factors including receptor activator of nuclear factor kappa-B ligand (RANKL), macrophage colony stimulating factor (M-CSF), interferon-gamma (IFN-γ) and tumour necrosis factor alpha (TNF-α) that stimulate the sequestration of blood monocytes in the tumour tissue and promote the formation of giant cells [8, 10, 17].

The giant cells are thought to be derived from the fusion of mononuclear stromal cells [8, 10]. They resemble osteoclasts in both their function and phenotype, and possess receptor sites for calcitonin [8, 10]. They are approximately 60 μm in size and have numerous nucleoli that are centrally located in the cytoplasm [8].

Malignant transformation is thought to occur in the mononuclear spindle shaped cell line as a result of genetic instability and uncontrolled proliferation [8]. These cells have increased expression of P53 protein and have alterations in various oncogenes, including C-myc, C-fos and N-myc [8, 20]. Noticeably, similar genetic alterations are frequently found in osteosarcoma [20-23].

Recognizing these rare tumours is extremely important, as they carry a very poor prognosis [2, 24]. This is especially true for primary malignant giant cell tumours. This situation is worse, as illustrated in this case, if the diagnosis is delayed or missed. Pre-operative planning is critical, as a misplaced biopsy site may miss the malignant element with the return of a benign diagnosis. In this regard MRI is of vital importance as it affords the surgeon the ability to choose the optimal biopsy site. The MRI scan of our patient clearly identified two distinctly different lesions. The two lesions were histologically proven to be a benign GCT with no evidence of malignancy and a conventional osteosarcoma. Seeing as this patient had no previous surgery or radiotherapy, and the coexistence of a sarcoma and a benign GCT in a single lesion was proven, this case represents a rare example of primary malignant transformation in a GCT.

The fact that this patient is HIV sero-positive may possibly be more than pure coincidence. A link between HIV infection and the development of certain malignancies have been established, including B-cell non-Hodgkin’s lymphoma and Kaposi sarcoma [25-27]. A possible association between HIV infection and osteosarcoma has also been suggested [28]. The pathogenesis of malignancy in HIV-infected individuals is either due to an indirect mechanism of immuno-suppression or direct mechanisms such as c-myc proto-oncogene expression during HIV infection. Further research into the relationship between HIV and the carcinogenesis of osteosarcoma is currently underway.
Conclusion
Malignant change in giant cell tumour of bone is rare. It is however important to be aware of this possibility and to recognize these lesions early. Magnetic resonance image (MRI) scanning provides vital information with regard to the choice of biopsy site and assist in making an accurate diagnosis and planning appropriate definitive treatment.

Conflict of Interest
The authors declare that they have no competing interests.

References