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Case report

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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

Introduction

Giant Cell Tumour (GCT) of bone is a benign but locally aggressive mesenchymal neoplasm that comprises 4-5% of primary bone tumours, and 20% of benign bone lesions [1, 2]. These tumours are intriguing and not well understood with regards to their genesis, progression or metastatic potential [3, 4].

Histologically, GCT's are characterized by mononucleated neoplastic stromal cells associated with uniformly distributed multinucleated osteoclast-like giant cells. The mononucleated cells are composed of two distinct cellular components, a spindle shaped major component and a minor component consisting of monocyte derived macrophages.

Despite being characterized/ classified as benign tumours, GCTs have the potential for pulmonary metastasis [5-7]. These metastases, however, do not herald malignant transformation, as they are histologically identical to the benign primary lesion, and have been hypothesized to be tumour emboli rather than true metastases [8].

Malignant change, on the other hand, is defined as sarcomatous change in the primary lesion. [9] Sarcomatous transformation of this nature is rare and only occurs in approximately 1% of cases [10-12]. Primary malignancy in GCT refers to the synchronous coexistence of a sarcoma and GCT within a lesion while secondary malignancy describes a sarcomatous growth in a previously treated, biopsy confirmed, benign GCT [1, 7-9, 11, 13, 14].

Secondary malignant transformation is far more common than primary malignancy and usually follows radiation therapy or multiple attempts at surgical resection of a documented benign GCT [5, 7, 8, 10, 12, 13, 15]. In this setting, the manifestation of Fibrosarcoma is three times more likely than osteosarcoma [15].

Primary malignant transformation is exceedingly rare and only a few examples exist in the literature [2, 7, 10, 13, 15]. In these cases, a malignant sarcoma is found juxtaposed to a benign GCT [5, 8, 10, 13]. The malignant component may

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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.

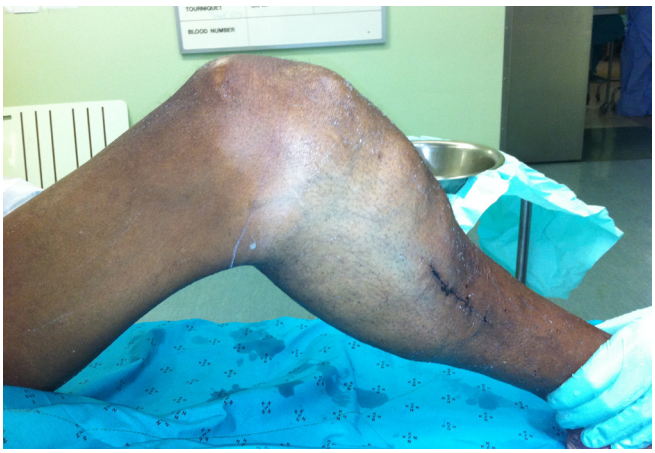

Figure 1 Patient with large tumour involving the proximal tibia and an 80-degree knee flexion contracture

The patient was known to be HIV positive on Highly Active Anti-retroviral Therapy (HAART) and systemic staging revealed a CD_4 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).

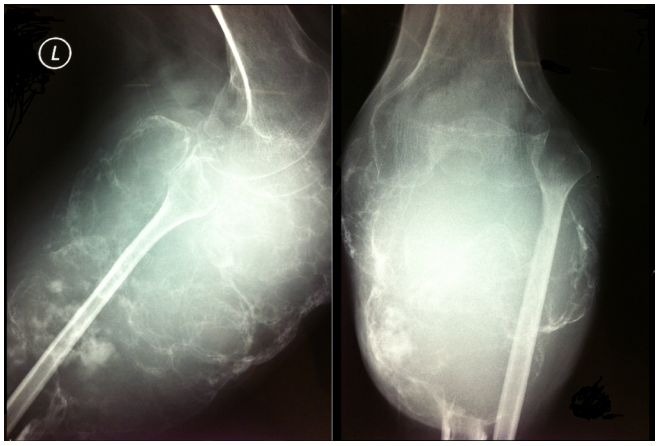

Figure 2 AP and lateral radiographs showing a large, geographic lytic lesion of the proximal tibia with cortical thinning, expansion and destruction.

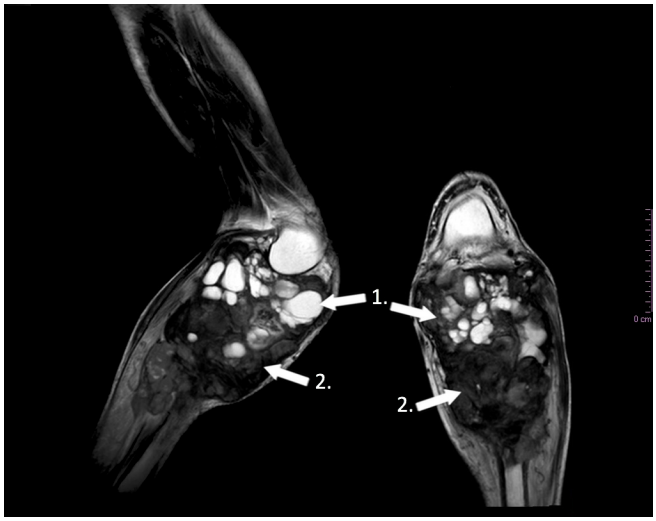

Figure 3 MRI scan with features of a giant cell tumour at arrow 1 and a osteosarcoma at arrow 2.

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). Due

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.

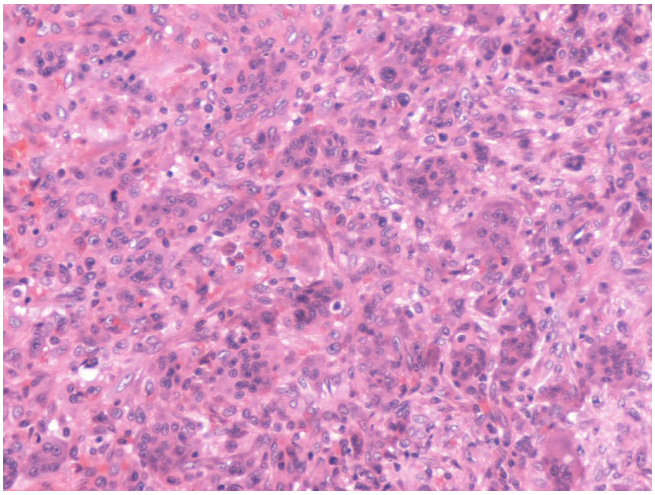

Figure 4 Histological specimen showing benign giant cell tumour.

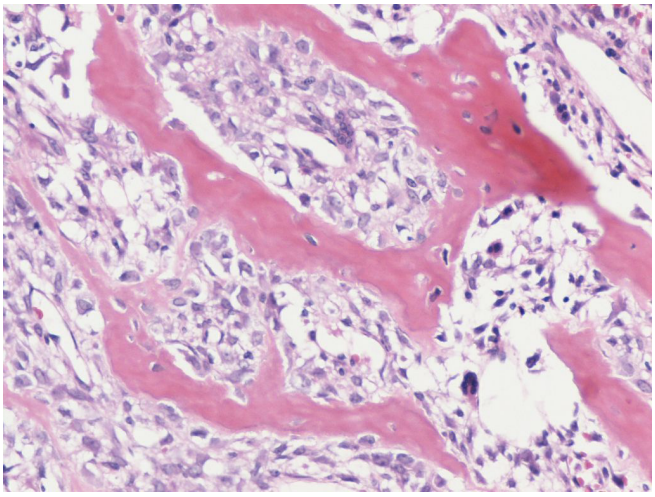

Figure 5 Histological specimen showing conventional osteosarcoma

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 compromised 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 immunosuppression 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

[1] BispoJúnior RZ, Camargo OP, Ida CM, Baptista AM, Ribeiro MB, et al (2009) Primary malignancy in giant cell tumor: a case report. Sao Paulo Med J 127:310–313.

[2] Nahal A, Ajlan A, Alcindor T, Turcotte R (2010) Dedifferentiated giant cell tumour of bone in the form of low-grade fibroblastic osteogenic sarcoma: case report of a unique presentation with follow-up. Curr Oncol 12:71–76.

[3] Faisham WI, Zulmi W, Mutum SS, Shuaib IL (2003) Natural history of giant cell tumour of the bone. Singapore Med J44:362–365.

[4] Zhen W, Yaotian H, Songjian L, Ge L, Qingliang W (2004) Giant-cell tumour of bone. The long-term results of treatment by curettage and bone graft. J Bone Joint Surg Br 86:212–216.

[5] Campanacci M, Baldini N, Boriani S, Sudanese A (1987) Giant-cell tumor of bone. J Bone Joint Surg Am 69:106–114.

[6] Dahlin DC (1985) Caldwell Lecture. Giant cell tumor of bone: highlights of 407 cases. AJR Am J Roentgenol144:955–960.

[7] Unni KK (2001) How to diagnose malignant giant cell tumor. Pathology Case Reviews 6 :33–37.

[8] Szendroi M (2004) Giant-cell tumour of bone. J Bone Joint Surg Br 86:5–12.

[9] HutterRv, Worcester JnJr, Francis Kc, Foote FwJr, Stewart Fw (1962) Benign and malignant giant cell tumors of bone. A clinicopathological analysis of the natural history of the disease. Cancer 15:653–690.

[10] Brien EW, Mirra JM, Kessler S, Suen M, Ho JK, et al (1997) Benign giant cell tumor of bone with osteosarcomatous transformation ('dedifferentiated' primary malignant GCT): report of two cases. Skeletal Radiol 26:246–255.

[11] Gulhane SR, Kate MS (2011) Sarcomatous transformation in a conventional giant cell tumour of femur. NJIRM 2:124–126.

[12] Sakkers RJ, van der Heul RO, Kroon HM, Taminiau AH, Hogendoorn PC (1997) Late malignant transformation of a benign giant-cell tumor of bone. a case report. J Bone Joint Surg Am 79:259–262.

[13] Bertoni F, Bacchini P, Staals EL (2003) Malignancy in giant cell tumor of bone. Cancer 97:2520–2529.

[14] Dahlin DC, Cupps RE, Johnson EWJr (1970) Giant-cell tumor: a study of 195 cases. Cancer 25:1061–1070.

[15] Hashimoto K, Hatori M, Hosaka M, Watanabe M, Hasegawa T, et al. (2006) Osteosarcoma arising from giant cell tumor of bone ten years after primary surgery: a case report and review of the literature. Tohoku J Exp Med 208:157–162.

[16] Schajowicz F (1993) Histological typing of bone tumours. World Health Organization, Berlin: Springer-Verlag, 20–22.

[17] Miller IJ, Blank A, Yin SM, McNickle A, Gray R (2010) A case of recurrent giant cell tumor of bone with malignant transformation and benign pulmonary metastases. Diagn Pathol 5:62.

[18] Goldring SR, Schiller AL, Mankin HJ, Dayer JM, Krane SM (1986) Characterization of cells from human giant cell tumors of bone. Clin Orthop Relat Res 204:59–75.

[19] Zheng MH, Robbins P, Xu J, Huang L, Wood DJ, et al. (2001) The histogenesis of giant cell tumour of bone: a model of interaction between neoplastic cells and osteoclasts. HistolHistopathol 16:297–307.

[20] Pompetti F, Rizzo P, Simon RM, Freidlin B, Mew DJ, et al. (1996) Oncogene alterations in primary, recurrent, and metastatic human bone tumors. J Cell Biochem 63:37–50.

[21] Gamberi G, Benassi MS, Bohling T, Ragazzini P, Molendini L, et al. (1998) C-myc and c-fos in human osteosarcoma: prognostic value of mRNA and protein expression. Oncology 55:556–563.

[22] Guo W, Wang X, Feng C (1996) P53 gene abnormalities in osteosarcoma. Chin Med J 109:752–755.

[23] Wu JX, Carpenter PM, Gresens C, Keh R, Niman H, et al. (1990) The proto-oncogene c-fos is over-expressed in the majority of human osteosarcomas. Oncogene 5:989–1000.

[24] Kapoor SK, Jain V, Agrawal M, Singh S, Mandal AK (2007) Primary malignant giant cell tumor of bone: a series of three rare cases. J Surg Orthop Adv16:89–92.

[25] Butel JS (2000) Viral carcinogenesis: revelation of molecular mechanisms and etiology of human disease. Carcinogenesis 21:205–426.

[26] da Silva SR, de Oliveira DE (2011) HIV, EBV and KSHV: viral cooperation in the pathogenesis of human malignancies. Cancer Lett 305:175–185.

[27] Ensoli B, Barillari G, Salahuddin SZ, Gallo RC, Wong-Staal F (1990) Tat protein of HIV-1 stimulates growth of cells derived from Kaposi's sarcoma lesions of AIDS patients. Nature 345:84–86.

[28] Marais LC, Ferreira N (2013) Osteosarcoma in Adult Patients Living with HIV/AIDS. ISRN Oncol. Doi: 10.1155/2013/219369.