Sarcomatous transformation in a conventional Giant cell tumour of femur

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Abstracts: Although giant cell tumour (GCT) is seen quite frequently, malignant giant cell tumour (MGCT) is a rare entity occurring in less than 1% of patients with GCT. It can develop as a primary (de novo) or a secondary form. Secondary malignant giant cell tumour occurs as a result of previous attempts at local control of a benign GCT i.e. post-surgical or post-irradiation. Malignant transformation has been very rarely reported in patients with GCT who have not received radiation treatment. We report a rare case of sarcomatous transformation in a benign giant cell tumour occurring six years after the primary surgery for GCT and without radiotherapy. This report of malignant spindle cell transformation of a conventional GCT of bone strengths the theory that there is a mesenchymal cell line in GCT which can spontaneously transform into sarcoma. The prognosis of such patients is poor because the malignancies are usually high grade sarcomas. Key Messages: Although giant cell tumour (GCT) is seen quite frequently, malignant giant cell tumour (MGCT) is a rare entity occurring in less than 1% of patients with GCT. It can develop as a primary (de novo) or a secondary form. The prognosis of such patients is poor because the malignancies are usually high grade sarcomas. [Gulhane S et al, NJIRM 2011; 2(4) : 124-126]

Key Words: Giant cell tumour of bone, Malignancy in giant cell tumour of bone, Postradiation sarcoma, Malignant spindle cell tumour

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Introduction: Giant cell tumour of bone is a relatively common tumour. It is characterized by the presence of multinucleated giant cells and benign spindle cells. [1] Malignancy in GCT is an extremely rare event, occurring in about 1.8% of GCTs in the bone. These malignancies can either be primary or secondary.[2] Approximately only 29 such well documented cases have been reported till date.[3, 4] Most of these cases have been primarily treated by radiation. On the other hand, secondary malignant tumour occurring in GCT without radiation therapy is extremely rare.[1] We report one such case of high-grade spindle cell sarcoma arising six years after primary surgery for benign GCT and who did not receive any radiotherapy.

Case History: A 50-year-old female presented with complaints of pain and swelling in the right knee joint along with inability to walk. The roentgenograph of the right knee joint showed an osteolytic lesion of approximately 6x5 cm size in the epiphysis of distal end of femur with well-circumscribed margins and pathological fracture in the distal end of the femur.(Fig.1&2)

The patient was treated with complete curettage along with radiotherapy for this recurrence.

After obtaining detailed past history it was revealed that the patient had similar complaints of the right knee joint six years back. It was diagnosed as benign GCT and treated with embolisation, curettage and bone grafting following which a repeat MRI scan suggested that tumor clearance was complete. Hence, no local radiotherapy was given to the patient at that time.

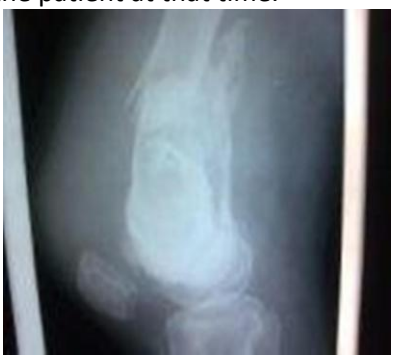

Fig 1: X-ray of Right Knee

Histopathology: After getting the detailed history we reviewed the histology slides of the lesion six years back. This lesion had the morphologic features of a classic giant cell tumour. Diagnostic areas were characterized by the mixture of stromal cells and multinucleated giant cells. Stromal cells had round, oval, or spindle-shaped nuclei without any hyperchromatism or pleomorphism. Giant cells were scattered uniformly throughout the lesion

and contained many nuclei that were similar to the nuclei of the stromal cells. No area of aggressive histological pattern was seen.

We received the curetted material from the present lesion. Macroscopically the material consisted of soft to firm, grey-white, friable tissue pieces. The curettage mass showed that on histology the lesion was a high grade spindle cell sarcoma. The spindle cells were arranged in interlacing bundles and sweeping fascicles. (Fig.3)

The nuclei showed high degree of pleomorphism, hyperchromatism, mitotic activity (10-15/10hpf), nuclear membrane irregularities and multinucleation. Areas of necrosis were also seen. However, areas of conventional GCT were not seen in this curettage material available. Hence, this lesion was diagnosed as a case of sarcomatous growth that occurred at the site of a previously documented benign GCT.

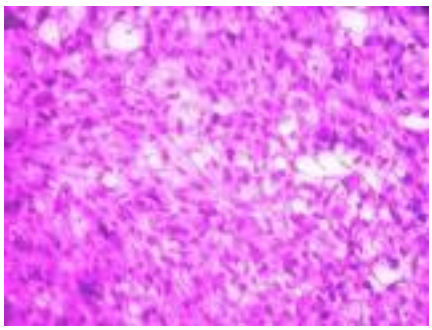

Fig 2: Malignant GCT

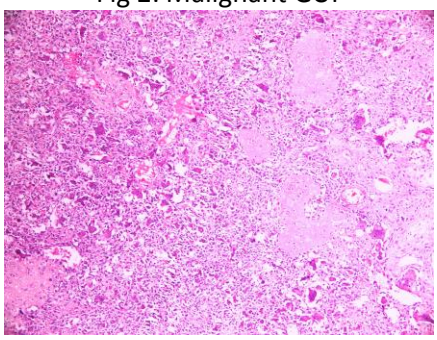

Fig 3: Benign GCT

Discussion: Giant cell tumors of bone is a common primary bone tumour which can exhibit a spectrum of clinical behavior from benign to frankly malignant with a capacity for local recurrence and tissue infiltration. Eighty per cent of cases of giant cell tumors occur in long bones and are often amenable to surgical excision. The axial skeleton accounts for only 8% of cases.[6] One to two per cent tumors may metastasize. Sarcomatous change in a previously histologically typical giant cell tumour is seen in less than 1% of cases without previous radiotherapy but of those irradiated 10% undergo sarcomatous transformation.[7]

Malignant giant cell tumour is a nonspecific term that has been used in the past to describe giant cell tumors with different degrees of anaplasia, giant cell-rich osteosarcomas, malignant fibrous histiocytomas containing multinucleated cells, locally aggressive giant cell tumors of bone, metastasizing benign giant cell tumors, and giant cell tumors with concomitant sarcoma either de novo or after definitive treatment.[2]

The term malignancy in giant cell tumour is proposed by Bertoni et al [2]. Two forms of such malignancies in GCT can be distinguished: a primary de novo i.e. Primary malignant giant cell tumor (PMGCT) and a secondary form i.e. secondary malignant giant cell tumor (SMGCT). A primary malignancy in giant cell tumour is a lesion in which there are areas of synchronous high-grade sarcomatous growth next to areas of benign giant cell tumour. [2, 4] A secondary malignancy in giant cell tumour is a metachronous high-grade sarcomatous growth superimposed on a previous, biopsy-verified, benign giant cell tumour that has been treated by either surgery or radiotherapy. The vast majority of secondary malignant GCT has a history of preceding irradiation of the lesion. Though, the radiotherapy - induced and post-surgical SMGCT may have different oncogenic mechanism, they cannot be distinguished from each other on the basis of radiographic and histological presentation.

Sakkers et al[7] proposed a noteworthy theory regarding the malignant transformation of giant cell tumour treated by curettage and bone grafting. The theory stated that in this situation, reparative proliferative changes that occur at the border of an area of dead bone could serve as the nidus for formation of a malignant tumor.[2] The present report of sarcomatous transformation of a conventional GCT of bone strengthens the theory

that there is a mesenchymal cell line in GCT that may spontaneously transform to sarcoma.

Bertoni et al[2] reviewed 17 cases of malignancy in giant cell tumour of which five were primary and twelve were secondary MGCTs of which half of the tumors were post-irradiation sarcomas. The average latent period between the diagnoses of giant cell tumour and SMGCT was 9 and 19 years for patients receiving radiotherapy and those with spontaneous transformation respectively.[2] The authors diagnosed more osteosarcomas among both primary malignancies (4 of 5 cases) and secondary malignancies (9 of 12 cases) whereas other authors found 3 times more fibrosarcomas than osteosarcomas among SMGCT cases.[4, 5]

Agrawal et al[3] have reported a case of osteosarcomatous transformation in a benign giant cell tumor. The lesion was present in the talus of the left ankle in a 13 year old male. Spontaneous malignant transformation is rare in a giant cell tumour; in addition a giant cell tumor arising in the bones of the hands and feet is in itself a rarity.

Studies have attempted to define a minimum latent interval between radiotherapy and secondary malignancy. In patients who had received radiotherapy at the site of the malignancy, it was found to be 1.7-15 years and in patients who did not receive previous radiotherapy it were 19 years.[2] There have been 29 well documented cases of malignancy in GCTs without radiation therapy in literature. In such cases of evolutionary malignancy the interval between discovery of GCTs and malignant transformation ranged from 1.4 years to 25 years (average 9.9 years).[1]

The prognosis of secondary malignancy in GCTs has been reported to be poor. Nascimento et al[7] reported that the prognosis seemed to vary according to the treatment regimen. Improvements in chemotherapy seem to contribute to the better prognosis. On the other hand, the prognosis after the appearance of malignancy is independent of the primary treatment, the histological type of the malignancy, or the duration between the onset of the primary benign GCT and the appearance of malignancy.[1]

Summary: Although the recurrence in conventional GCT is common, malignancy in these cases is an extremely rare event. Moreover it is compounded by the fact that the prognosis of these cases is very poor. Hence it is imperative that such malignant transformations should be recognized at an early stage so that adequate aggressive therapeutic protocol can be administered. To conclude, we would like to stress that clinicians as well as pathologists must follow the patient with recurrences in conventional GCT treated either with or without radiotherapy over a long period keeping in mind the risk of developing sarcomas in future.

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