

## GIANT CELL-RICH OSTEOSARCOMA: A CASE REPORT

KEIJI SATO<sup>1</sup>, SHIGEKI YAMAMURA<sup>1</sup>, HISASHI IWATA<sup>1</sup>, HIDESHI SUGIURA<sup>2</sup>,  
NOBUO NAKASHIMA<sup>3</sup> and TETSURO NAGASAKA<sup>3</sup>

<sup>1</sup>Department of Orthopaedic Surgery, Nagoya University School of Medicine

<sup>2</sup>Division of Orthopaedic Surgery, Nagoya Memorial Hospital

<sup>3</sup>Division of Clinical Laboratory, Nagoya University Hospital

### ABSTRACT

This report discusses a rare case of giant cell-rich osteosarcoma. The patient, a 19-year-old male, was diagnosed with a metadiaphyseal osteolytic lesion when he consulted a local doctor complaining of motion pain without swelling. Radiography revealed a geographic osteolytic lesion, cortical thinning and ballooning without obvious cortical destruction. However, a fine onion skin-like periosteal reaction was observed on the lateral side of the femur. The transitional zone was narrow and endosteal scalloping was also noted. Needle biopsied material clearly showed nuclear atypism of the stromal tumor cells with numerous osteoclast-like giant cells. Using a combination of pathological examination, radiography, computed tomography (CT) and magnetic resonance imaging (MRI), a diagnosis of giant cell-rich osteosarcoma was reached. After chemotherapy, resection and limb salvage surgery with an autogeneous autoclaved bone graft, a vascularized fibular graft were performed, and the patient has shown excellent limb function without local recurrence or distant metastasis during the past 72 months.

Key Words: Giant cell-rich osteosarcoma, Autoclaved bone graft, Vascularized fibular graft

### INTRODUCTION

Giant cell-rich osteosarcoma, first described by Bathurst et al.,<sup>1)</sup> is a rare variant of osteosarcoma, accounting for 1 to 3% of conventional osteosarcoma cases, though differential diagnosis from malignant giant cell tumor (GCT) is difficult in some cases.

### CLINICAL INFORMATION

#### History of the present illness:

The patient was a 19-year-old male whose chief complaint was left distal thigh pain. The pain occurred during his job in July 1989 and gradually worsened until the middle of August when the pain continued at night. The patient consulted a local doctor who detected an abnormal shadow on a radiograph of the left femur. Needle biopsy was done on August 19, and the diagnosis of a giant cell tumor in the distal metadiaphyseal region of the left femur was made. The patient was then referred to Nagoya University Hospital on September 5, 1989.

Correspondence: Dr. Keiji Sato, Department of Orthopaedic Surgery, Nagoya University School of Medicine, 65 Tsurumai-cho, Showa-ku, Nagoya 466, Japan

Tel: 81-52-741-2111, ext 5081 Fax: 81-52-744-2260

**Physical examination:**

Physical examination revealed a hard, bone like protrusion on the distal part of the left femur with atrophy of the quadriceps muscle. There was slight tenderness over the bony lump with local warmth. A limp was present, but the range of the motion of the hip and knee joint was normal. The inguinal lymph nodes could not be palpated.

**Characteristic imaging:**

A radiograph of the femur clearly disclosed a geographic osteolytic lesion with a sharp margin in the distal metadiaphyseal region. The transitional zone was narrow. Endosteal scalloping was observed; however, obvious cortical destruction was not detected. A fine onion skin-like periosteal reaction was observed on the lateral side of the femur. Soft tissue extension could not be detected (Fig. 1). CT clearly demonstrated that the cortex was thinned and ballooned without destruction (Fig. 2). MR images (GE Signa 1.5T) showed that the lesion had a low signal intensity on T1-weighted images, intermediate intensity mixed with low signal intensity on proton density images and very high signal intensity (suggestive of hematoma) with a low signal intensity area on the T2-weighted images (Fig. 3).

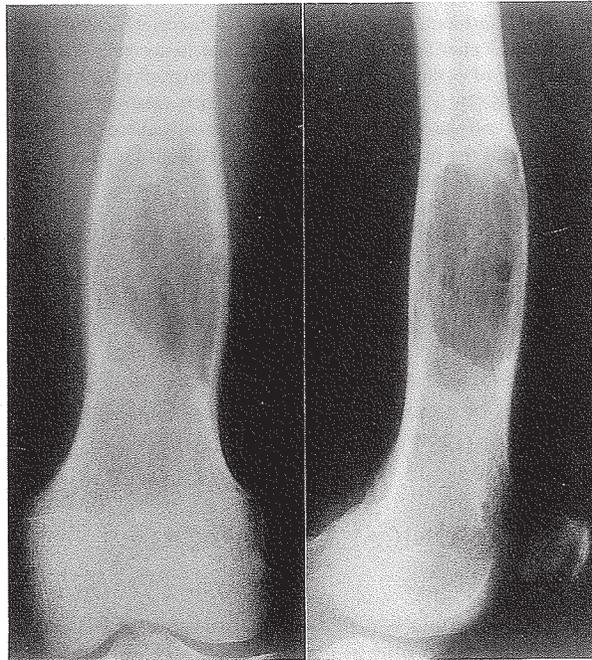


Fig. 1. Radiography of the left femur in antero-posterior and lateral views clearly disclosed a geographic osteolytic lesion with a sharp margin shown in the distal metadiaphyseal region. The transitional zone was narrow. Endosteal scalloping was observed and a faint onion skin-like periosteal reaction was also found on the lateral side of the lesion.

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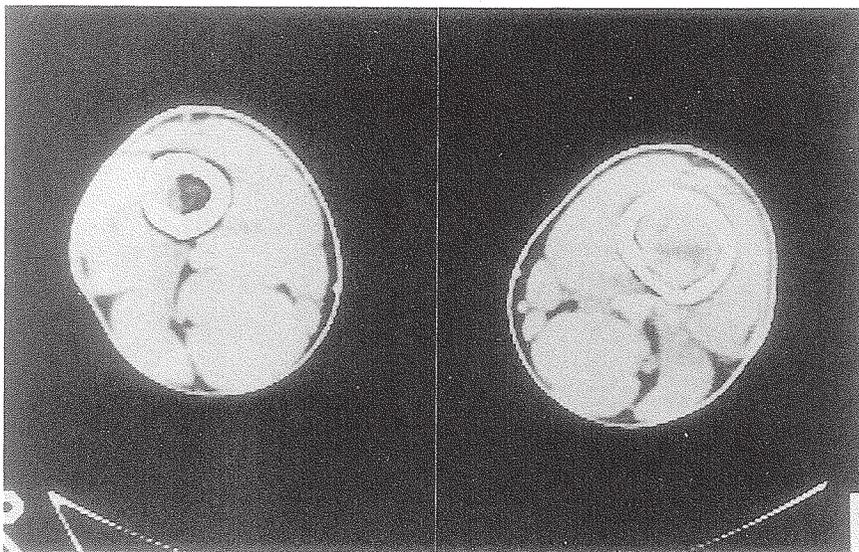


Fig. 2. CT demonstrated the expanded cortex without destruction.

#### Pathological findings:

The pathological findings of the needle-biopsied material revealed numerous benign osteoclast-like giant cells in the tumor tissue, but the neoplastic cells showed atypism in their nuclear form, and few mitoses were found. Also in the tumor matrix, osteoid was partially demonstrated; however, obvious bone formation was not detected (Fig. 4). Based on these findings, the diagnosis was a giant cell-rich osteosarcoma.

#### Treatment:

First, intra-arterial cisplatin (100 mg/meter<sup>2</sup>), was administered and then limb salvage surgery was performed, using an autogenous autoclaved bone graft in combination with a vascularized fibular graft, after wide resection of the lesion. Postoperative chemotherapy was continued until August 1990, with high-doses of methotrexate (10 gr/meter<sup>2</sup>) except for the use of cisplatin (100 mg/meter<sup>2</sup>) on day 1 and adriamycin (35 mg/meter<sup>2</sup>) on days 1 and 2. The postoperative follow-up period to date has been 72 months, and the patient remains disease-free.

#### Function of salvaged limb:

The function of the left knee joint was evaluated. Flexion was 40 degrees and extension was 0 degrees. Limb shortening was 2 cm. The patient returned to his previous job, maintaining a normal walking level without support.

#### Radiograph in follow-up period:

37 months after surgery, a radiograph showed a beautifully formed bone bridge between the proximal femur and the vascularized fibula at the proximal site of the autoclaved bone graft. At the distal site, the gap between the distal femur and the autoclaved bone was completely filled

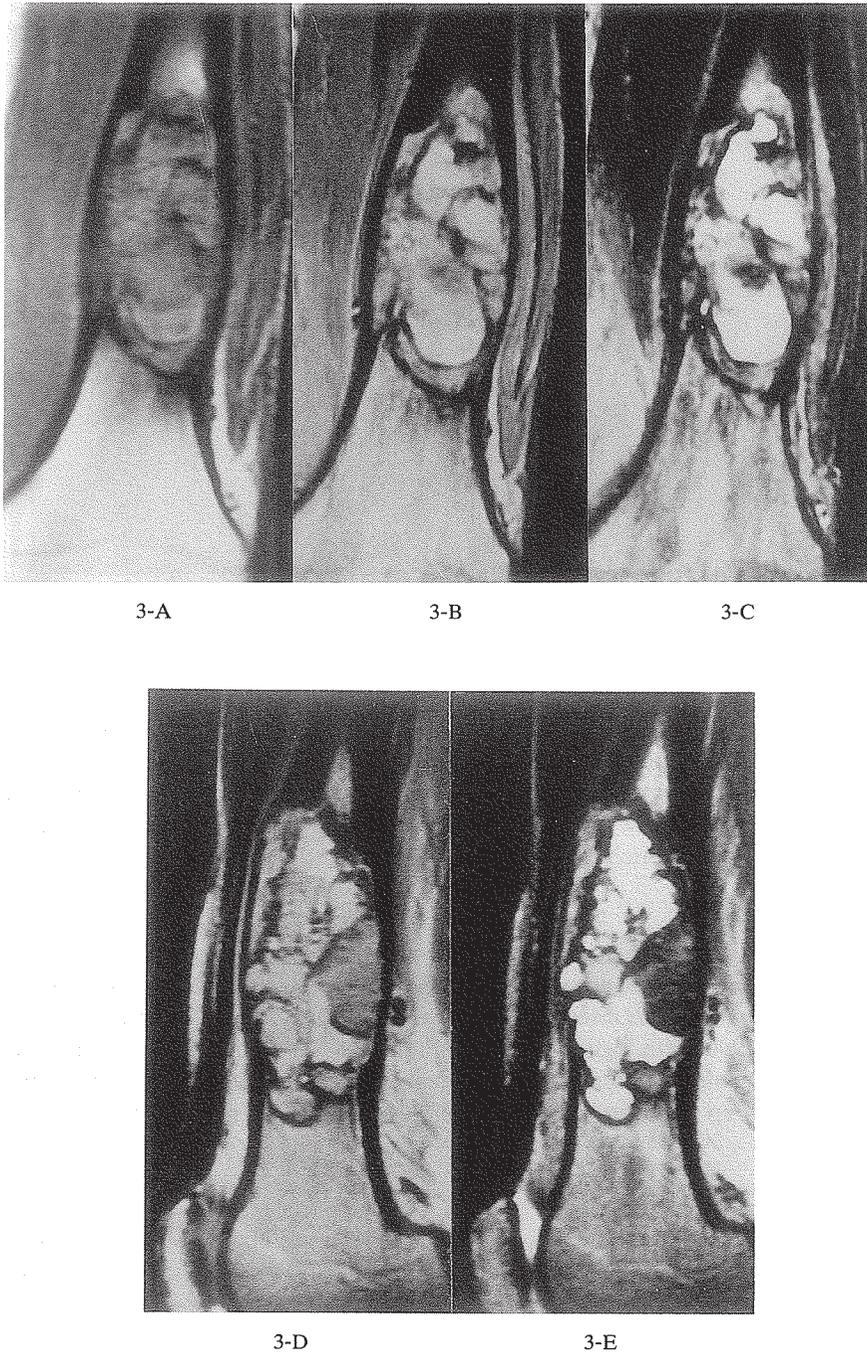


Fig. 3. MR images of the coronal plane of the femur (3-A: T1-weighted images, TR400/TE20. 3-B: Proton density, TR2000/TE20. 3-C: T2-weighted images, TR2000/TE80) On T1-weighted images, the lesion showed a homogeneous low signal intensity, but the T2-weighted images demonstrated a marked high signal intensity mixed with an area of low signal intensity. MR images of the sagittal view (3-D: Proton density, TR2000/TE20. 3-E: T2-weighted images, TR2000/TE80) demonstrated the same changes.

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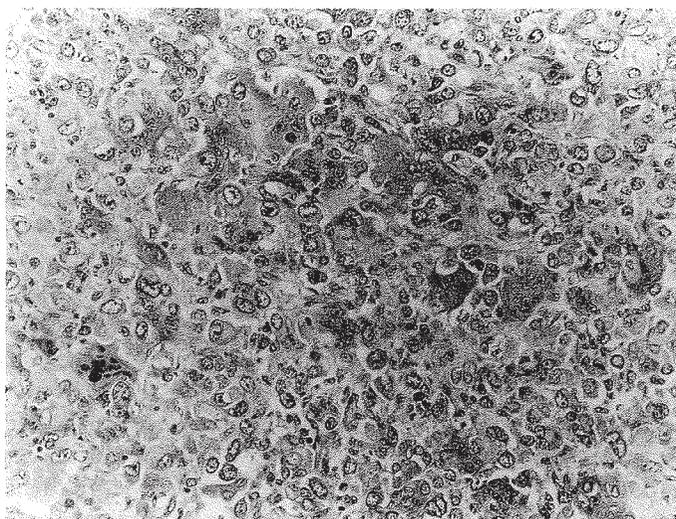


Fig. 4. The pathological findings of the needle biopsied material revealed numerous osteoclast-like giant cells in the tumor tissue, but the tumor cells showed atypism in their nuclear form, and few mitoses were found. In the tumor matrix, osteoid was clearly and partially demonstrated.

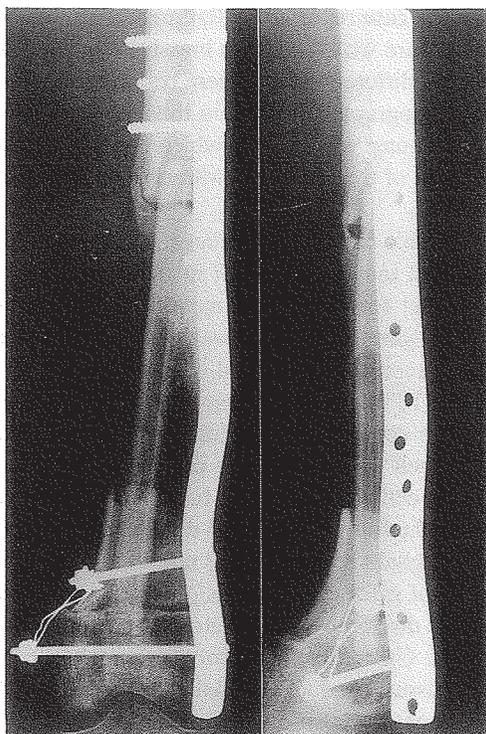


Fig. 5. Radiography, 37 months after surgery, showed complete union between the host bone, autoclaved bone and vascularized fibula.

with new bone (Fig. 5). The autoclaved bone has gradually been absorbed and sideways enlargement of the fibular graft has also been observed.

## DISCUSSION

Giant cell-rich osteosarcoma, first described by Bathurst *et al.*,<sup>1)</sup> has been considered an extremely rare variant of osteosarcoma, and its incidence was reported to make up 3% of all osteosarcoma cases. However, no case reports of giant cell-rich osteosarcoma have been published since the report of Bathurst *et al.*

**Radiographic differentiation:** Besides the characteristic histology of this unique variant, Bathurst *et al.*<sup>1)</sup> described the typical radiographic pattern of osteoclast-rich osteosarcoma as follows: "An ill-defined margin surrounds a predominantly lytic lesion of the diaphysis or metaphysis of the femur or tibia of a young patient, a soft-tissue mass is usually not present and the periosteal reaction is weak." Mirra<sup>2)</sup> described in his textbook that benign osteoclast-like giant cells were present in diffuse and massive quantities in 1 to 2% of conventional osteosarcoma cases. He reported that three radiographic differential points were needed to differentiate GCT-like variants of osteosarcoma from true GCT: (1) metaphyseal or diaphyseal centering versus epiphyseal centering, (2) Codman's triangle, (3) any radiographic intralesional fluffs. Radiography in this case revealed a metadiaphyseal location in the left femur, along with a geographic osteolytic pattern with endosteal scalloping and cortical ballooning without obvious cortical destruction. A faint onion skin-like periosteal reaction was also noted, especially on the lateral side of the left femur; however, soft tissue extension was not shown. The radiographic pattern of this case was fully consistent with the case reported by Bathurst *et al.*,<sup>1)</sup> suggesting that this tumor lesion has a slowly progressive nature with low grade invasive tendency. The metadiaphyseal location in this case is a valid way of differentiating it from true GCT, which locate exclusively in the epiphysis or epimetaphysis. Radiographic changes in this case show a clear differentiation from conventional osteosarcoma in young adolescents, which typically show rapid invasion and destruction in the metaphyseal area of the long bone with certain periosteal reaction and soft tissue extension into surrounding tissue.

**Histological differentiation:** This case was first diagnosed by a pathologist in a local hospital as an atypical case of a giant cell tumor because of its abundant giant cells. However, considering the nuclear atypism, osteoid formation and metadiaphyseal location, diagnosis as a true giant cell tumor or a malignant giant cell tumor was not made, and the case was finally diagnosed as giant cell-rich osteosarcoma. Troup *et al.*<sup>3)</sup> pointed out that some foci of osteoclast-type giant cells were present in 13% of the osteosarcoma cases they investigated. However, the main lesions in these cases were considered to be conventional types of osteosarcoma, and the osteosarcoma cases with giant cell foci were easily differentiated from giant cell-rich osteosarcoma. Primary malignant giant cell tumors of the bone are histologically distinguishable from giant cell-rich osteosarcoma in the following ways:<sup>4)</sup> microscopic examination reveals that direct formation of osteoid by the malignant spindle cells is not seen in primary malignant giant cell tumors of the bone, and an area of giant cell tumor is present in addition to verified areas of sarcomatous stroma. Mirra<sup>2)</sup> also disclosed two differentiating histological points between giant cell-rich osteosarcoma and true GCT. One difference was anaplasia of some stromal cells and the other was osseous tumor tissue production. Malignant fibrous histiocytoma contains small foci of osteoid in half of the cases, and also contains multi-nucleate tumor cells (malignant giant cells). However, the basic proliferating component is a fibrohistiocytic cell exhibiting a storiform

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or cartwheel pattern; this pattern helps to differentiate malignant fibrous histiocytoma from giant cell-rich osteosarcoma.<sup>5)</sup>

Recently Hill et al.<sup>6)</sup> reported that osteoblast cells or human osteosarcoma cells (MG63) mediate insulin-like growth factor (IGF)-1 and -II stimulation of osteoclast formation in a culture system. Giant cell-rich osteosarcoma might be interpreted as a unique osteosarcoma which produces rich IGFs, thereby stimulating osteoclast differentiation. From now on, research efforts should focus on humeral factors produced by osteosarcoma cells which might moderate both the histology of osteosarcoma and the natural course of the osteosarcoma bearing host.

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