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Dedifferentiated Parosteal Osteosarcoma of the Femur
- A Case Report -

Hye-Rim Park, Yong-Koo Park*, Joon-Dong Jang, Eun-Sook Nam, Jin-Hee Sohn**

*Department of Pathology and Orthopedic Surgery**,
College of Medicine, Hallym University, Anyang, Korea
Department of Pathology, College of Medicine, Kyung-Hee University, Seoul, Korea**

- Abstract -

We present a case of parosteal osteosarcoma of the femur with secondary dedifferentiation. This 57-year-old woman was radiologically diagnosed as a parosteal osteosarcoma in 1987. In 1992, excisional biopsy revealed a classical parosteal osteosarcoma with diploidy DNA pattern. In 1998, she revisited due to a recurrent tumor with pathologic fracture. The resected specimen showed a classic parosteal osteosarcoma with area of dedifferentiation, showing high-grade spindle cell sarcoma. This dedifferentiated area revealed aneuploidy cell population on DNA flow cytometry. This case reminds us that not all parosteal osteosarcomas are low-grade lesions. Some low-grade lesions may dedifferentiate to become high-grade tumors after inadequate excision.

Key Words : Osteosarcoma, Parosteal, Dedifferentiation

INTRODUCTION

Parosteal osteosarcoma is a surface osteogenic sarcoma characterized by a low-grade malignant spindle-cell tumor with a well-formed bone production[2,7,11,12,14]. The usual course of typical parosteal osteosarcoma is accepted as a gradual growth of tumor mass with a strong tendency to recur locally, but a lesser tendency to distant metastasis and death[2,3,7,11,12,14]. In 1979, Dunham et al.[3] described a large classical parosteal osteosarcoma, which histologically showed areas of high-grade osteosarcoma transformation. Previous studies of parosteal, or juxtacortical tumors have included mention of the occasional occurrence of high-grade anaplastic tumors that do not fit the usual patterns of parosteal osteosarcoma. In most of these reports, a low-grade parosteal osteosarcoma "dedifferentiated" after multiple recurrences to high-grade tumor[3,12,14].

Dedifferentiation of conventional parosteal

※통신저자 : Hye-Rim Park, M.D.
Department of Pathology, Hallym University Sacred Heart Hospital
#896 Pyungchon-dong, Dongan-ku, Anyang, 431-070, Korea
Tel : 0343) 380-3935, Fax : 0343) 381-9646

osteosarcoma may occur as either primary or secondary event. When it occurs as a primary event, a high-grade sarcoma is juxtaposed with the low-grade, fibro-osseous component. In secondary transformation, dedifferentiation occurs after multiple recurrences of a low-grade tumor[3,12,14].

We present a case of parosteal osteosarcoma of the femur dedifferentiated to a high-grade sarcoma with aneuploidy cell population in a recurrent tumor 11 years later.

CASE REPORT

In 1987, this 57-year-old woman had pain and swelling in her right knee for several months. Radiographs revealed a large, radiodense lesion with an irregular cortical margin arising in the posterior aspect of the right distal femur(Fig. 1). The radiologic impression was parosteal osteosarcoma. She refused surgical treatment at the time. Five years later in 1992, a computed axial tomography scan revealed an expansile homogeneous lesion of high density with a medullary involvement. An excision was done on the protruding lesion. We made a diagnosis of grade 1 parosteal osteosarcoma and recommended a wide local resection, including normal tissue.

In 1998, six years later, she revisited due to a pathologic fracture. Physical examination revealed tenderness, swelling, limitation of motion, and crepitus on her distal femur. The anteroposterior and lateral views of right knee showed a large osteolytic and sclerotic lesion as well as a pathologic fracture(Fig. 2). A magnetic resonance image showed a huge soft tissue mass of heterogeneous signal intensity, protruding to the popliteal fossa(Fig. 3). On the contrast enhancement, it showed a heterogeneous enhancement. Above knee amputation was done after an open biopsy. On chest CAT scan, there was no metastatic lesion. After the final diagnosis, the patient was received the systemic chemotherapy including Adriamycin and Dacarbazine.

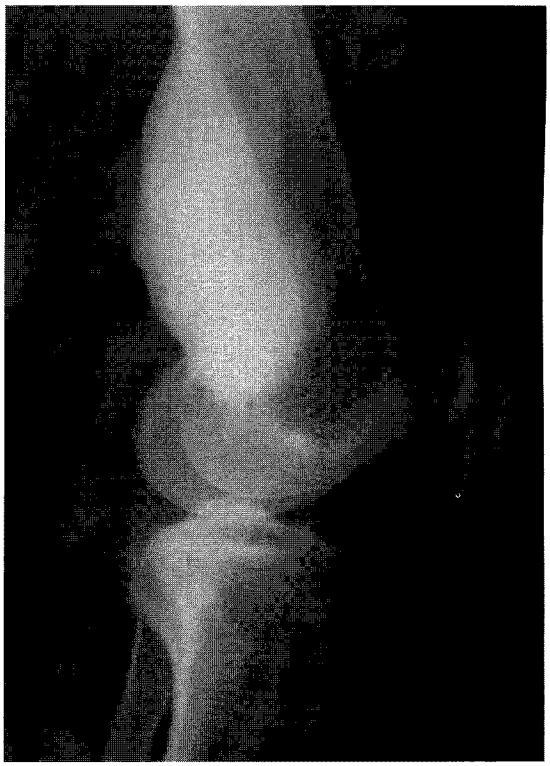

Fig. 1. Lateral view of right knee shows a large, radiodense lesion protruding to the popliteal fossa.

PATHOLOGY

In 1992, the lesion was composed of irregular, anastomosing mature bony trabeculae and low-grade fibroblastic lesion between them(Fig. 4). Cellular proliferation was hypocellular, with abundant collagen between individual tumor cells. The spindle cells showed minimal cytologic atypia. The tumor cells were diploidy cell population on flow cytometry(Becton Dickinson, CellFIT cell-cycle analysis version 2.01.2). We diagnosed

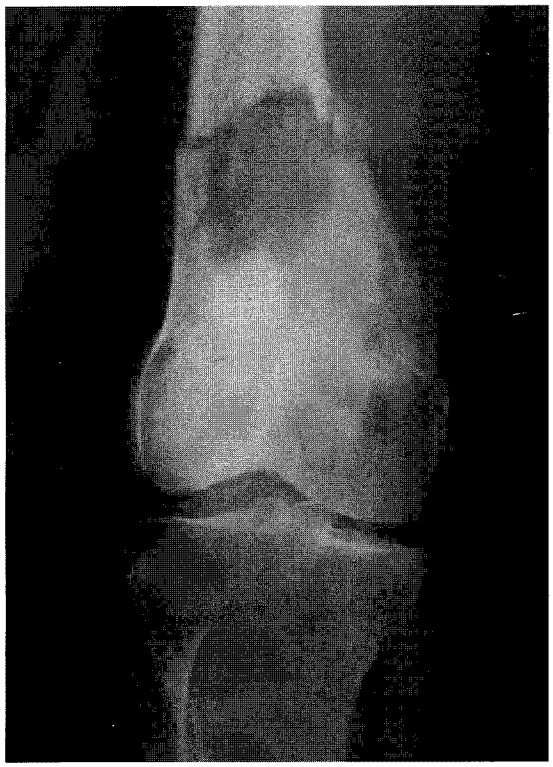

Fig. 2. Anteroposterior view of right knee shows a large osteolytic and sclerotic lesion as well as a pathologic fracture.

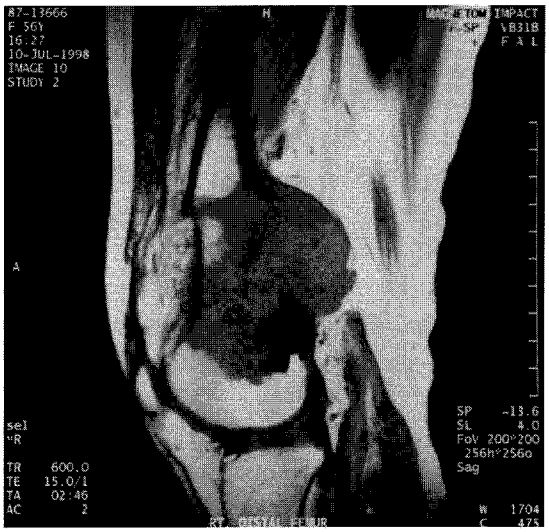

Fig. 3. T1 weighted MR image shows a huge soft tissue mass of heterogeneous signal intensity.

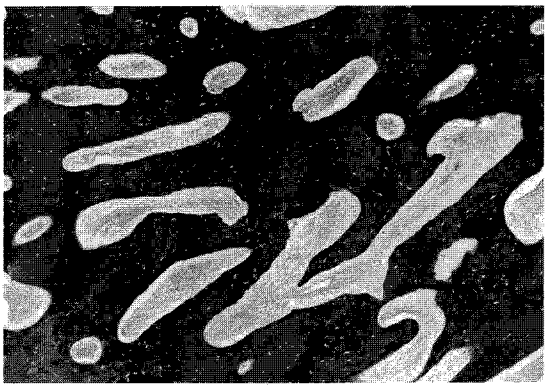

Fig. 4. Microscopically, the lesion is composed of anastomosing mature bony trabeculae and low-grade fibroblastic lesion(H&E, ×100).

it as grade 1 parosteal osteosarcoma.

In 1998, the resected specimen of her right femur revealed a huge gritty and hemorrhagic soft tissue mass as well as a pathologic fracture. It filled the medullary cavity and extended into the surrounding soft tissue. Histologically, most of the lesion showed typical grade 1 parosteal osteosarcoma. In addition to this typical parosteal osteosarcoma, the low-grade lesion abruptly changed to high-grade spindle cell sarcoma in some areas(Fig. 5). This area was composed of short fascicles of pleomorphic, hyperchromatic spindle cells, mimicking malignant fibrous histiocytoma. There were a lot of tumor giant cells, malignant tumor osteoid, and calcification(Fig. 6). The tumor infiltrated surrounding adipose tissue in an irregular fashion. This dedifferentiated area revealed aneuploidy cell population on DNA flow cytometry. We diagnosed parosteal osteosarcoma with secondary dedifferentiation in a recurrent tumor.

DISCUSSION

Parosteal osteosarcoma was first described as a distinct clinico-pathologic entity in 1951[4] and is distinguished from ordinary osteosarcoma by its characteristic clinical,

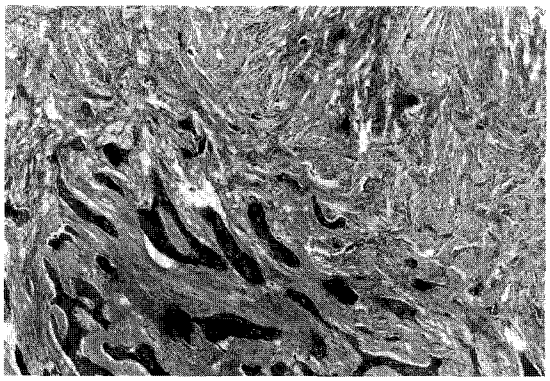

Fig. 5. Typical low grade lesion abruptly changes to high-grade spindle cell sarcoma in some areas(H&E, ×40).

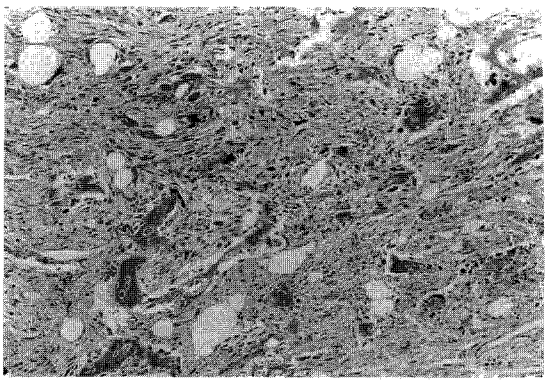

Fig. 6. High-grade lesion is composed of anaplastic tumor cells and malignant tumor osteoid, infiltrating surrounding soft tissue(H&E, ×200).

radiologic, and histologic presentation and its more favorable course[9,14]. Differences in clinical presentation include the advanced age of the patient and the longer duration of symptoms like the presented case. The criteria for diagnosis of parosteal osteosarcoma are that, roentgenographically, the lesion has arisen from the surface of the bone and that, histologically, the tumor is well differentiated; it is characterized by well-formed osteoid within a spindle-cell stroma; and when there is medullary involvement, less than 25 percent of the medullary cavity is affected[8,9].

The initial x-rays of this case in 1987 showed a radiologically typical parosteal osteosarcoma. Histologically, the excisional biopsy in 1992 revealed a typical grade 1 parosteal osteosarcoma. Eleven years after her first visit, in 1998, dedifferentiation of the lesion to a high-grade osteosarcoma has occurred. Microscopically, well-differentiated fibrous and bony tissues coexist with a component of high-grade osteosarcoma. Because of the long clinical course with no metastasis, this case seems to demonstrate a dedifferentiation of a typical parosteal osteosarcoma.

Dedifferentiation in a conventional parosteal osteosarcoma is not uncommon(up to 20 percent of the patients) and is associated with a poor prognosis[1,5,7,8,10,12-14]. Cross-sectional imaging studies in dedifferentiated cases demonstrated medullary involvement in 22 percent, unmineralized soft-tissue mass peripheral to the mineral component in 51 percent, and adjacent soft-tissue invasion in 46 percent[8]. Incomplete resection is associated with an increased risk in local recurrence and the dedifferentiation markedly increases the risk of metastasis[8].

The incidence of dedifferentiation in low-grade parosteal osteosarcoma supports the importance of correct diagnosis and treatment when the lesion is first seen. Inadequate initial surgical treatment in 1992 allowed for recurrence and dedifferentiation in this case. Rapid growth of a lesion or severe pain suggests dedifferentiation[14]. Selective sampling of radiolucent areas, the tumor's soft tissue component[6], or areas of localized hypervascularity as seen on angiography[12] increase the likelihood of obtaining tissue from the high-grade component in the biopsy material.

An interesting finding of van Oven et al.[9] is the aneuploid DNA stemline in the dedifferentiated tumor. In the present case, we performed DNA flow cytometry on both conventional and dedifferentiated components.

The primary tumor and conventional area in a recurrent tumor revealed diploid DNA pattern. In contrast, the dedifferentiated component revealed aneuploidy cell population. The presence of an aneuploid stemline represents a tumor clone with more aggressive properties and greater metastatic ability than a less malignant euploid tumor cell population[9].

For local control of the tumor and prevention of recurrence with potential dedifferentiation, the current approach for parosteal osteosarcoma is a wide local resection to obtain a wide surgical margin that includes an envelope of surrounding normal tissue. Treatment for dedifferentiated parosteal osteosarcoma is similar to that for conventional high-grade osteosarcoma. The prognosis appears to be similar to that of patients with high-grade intramedullary osteosarcoma[14].

In conclusion, not all parosteal osteosarcomas are low-grade lesions. A proportion of them present as high-grade tumors, and some low-grade lesions may dedifferentiate to become high-grade tumors after inadequate excision[14].

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= 국문초록 =

대퇴골에 발생한 역분화성 방골성 골육종
- 증례 보고 -

한림대학교 의과대학 병리학교실, 정형외과학교실**
경희대학교 의과대학 병리학교실*

박혜림 · 박용구* · 장준동 · 남은숙 · 손진희**

57세 여자 환자의 대퇴골 원위부에 발생한 방골성 골육종이 이차적 역분화를 일으킨 예를 치험하여 이를 보고하고자 한다. 57세 여자 환자가 1987년 방사선 소견상 대퇴골 방골성 골육종으로 진단되었고, 1992년 절제 생검을 시행한 결과 통상적인 방골성 골육종이었고, 이배수성의 DNA를 나타내었다. 1998년 환자는 병적 골절이 동반된 재발성 종양으로 재입원 하였다. 절제된 종양은 통상적인 방골성 골육종의 부위뿐만 아니라, 고등급의 방추성 세포 육종의 특징을 보이는 역분화 부위가 혼재하여 있었다. 이러한 역분화 부위는 유세포 측정을 이용한 DNA 검사상 이수배수성을 나타내었다. 본 증례를 통하여 모든 방골성 골육종이 저등급 병변은 아니고, 일부의 저등급 병변이 불충분한 절제 후에 고등급의 종양으로 역분화할 수 있음을 알 수 있다.