Giant Cell-Rich Osteosarcoma Simulating Giant Cell Tumor of Bone

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A seventeen-year-old boy was referred to our hospital, complaining of continuous pain of his left wrist joint. Plain roentgenogram showed an osteolytic lesion at the distal end of the radius. An operation in which the tumor was curetted was performed suspecting giant cell tumor. Pathological diagnosis was of a giant cell tumor. One month after the operation, radiological findings showed local recurrence with an expanded lysis. Wide resection of this tumor followed by a vascularized fibular graft was performed. Six months after the second operation, soft part swelling suggesting local recurrence was again prominent. Upper arm amputation was performed because of the bad local condition. The pathological diagnosis of these operative specimens was of giant cell tumor similar to that of the initial specimen. Multiple metastases appeared eight months after the third operation. In spite of intensive treatment, the patient died of respiratory failure. Autopsy revealed that pathological features from metastatic specimens were similar to those of osteosarcoma, not giant cell tumor. When we encounter patients presenting with a giant cell tumor, especially when they are younger than the age at which such lesions usually occur, we should bear in mind the possibility of an osteosarcoma and perform intensive chemotherapy and surgery.

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Introduction

Giant cell tumor of bone comprises a characteristic mixture of varying numbers of multinucleated giant cells dispersed in mononuclear stromal cells.1,2 Its pathological features are utilized to assess clinical behavior.3 However, the prognostic significance of histological grading remains controversial.4~6 Moreover, local aggressiveness on clinical or radiological grounds cannot be correlated with any specific findings.4,6 Metastases are rare events: pulmonary metastases have been reported in less than 5% of patients with conventional giant cell tumor of bone.5~8 It is sometimes stressful for clinicians to decide how to treat giant cell tumor of bone.

Giant cell-rich osteosarcoma is a rare tumor subtype accounting for only 1~2% of all osteosarcomas.9,10 Incorrect histological diagnosis as a giant cell tumor may be made because of similarities between these tumors. Clinical information including the prognosis and optical treatment is limited.10 This report describes a case of rare giant cell-rich osteosarcoma with an aggressive clinical course and rapidly fatal outcome.

Case Report

A seventeen-year-old boy was referred to our hospital on August 1991 complaining of continuous pain of his left wrist joint. He had initially noted the pain in May 1991 while playing volleyball. On physical examination, his wrist joint showed severe swelling with local heat and tenderness; the range of motion of his left wrist joint was slightly limited. Laboratory data showed only a slightly elevated serum alkaline phosphatase activity. Plain roentgenogram showed an osteolytic lesion at the distal end of the radius (Fig. 1). Arteriography demonstrated hypervascularity at that area. An operation by which the tumor was
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curetted was performed in August 1991. Investigations of other lesions, such as bone or extraskeletal metastases, were not performed at that time because giant cell tumor was suspected because of clinical and radiological findings. Pathological diagnosis was indeed of a giant cell tumor with spindle-shaped or ovoid-shaped stromal cells, a few mitotic figures and osteoclastic type giant cells (Fig. 2). In September 1991, radiological findings of his left wrist joint showed local recurrence with an expanded lysis and loss of the sclerotic margin (Fig. 3). Wide resection of this tumor followed by a vascularized fibular graft with fusion of the left wrist joint was performed in October 1991. Pathological findings were similar to those at the time of the initial operation. However, in April 1992, soft part swelling suggesting local recurrence was again prominent (Fig. 4). We consulted pathologists to confirm that pathological findings were truly compatible with those of giant cell tumor because this local recurrence was unexpectedly early. They unanimously replied that these findings were compatible with those of giant cell tumor, not those of osteosarcoma. Because of deterioration in the clinical findings, we started chemotherapy using pirarubicin, ifosfamide and carboplatin; despite that treatment, local swelling worsened with severe pain. Upper arm amputation was performed in September 1992 because of the bad local condition. Pathological findings were similar to those of the previous two operations. In December 1992, the patient complained of low back pain. Plain roentgenography showed a compression fracture of the third lumbar vertebral body. Chest roentgenography also showed pulmonary metastasis at that time. In June 1993, the patient became unable to walk because of spinal cord palsy below the level of...
the tenth thoracic spine. Radiation therapy, total 50 Gy, was administered to the lumbar spine in June 1993. In October 1993, 99mTc-DMSA scintigraphy showed increased uptake at skull, sternum, cervical spine, thoracic spine, lumbar spine, and pelvis. Chemotherapy using high-dose methotrexate, cisplatin and ifosfamide was continued; little effect was obtained. The patient died in January 1995 of respiratory failure. At autopsy, metastases were found in the bilateral upper pulmonary lobes and posterior thoracic walls, thoracic and lumbar spines, sacral bone, lumbar spinal cord, and skull. Metastases of the lung and posterior pulmonary walls included hemorrhagic foci and ossifications. The metastases comprised multinucleated giant cells interspersed with spindle-shaped stromal cells showing a compact or striform pattern with a few mitoses. Little atypism of the stromal cells differed from that of the operative specimens. However, tumorous osteoid formation was prominent compared with that of the operative specimens, especially in pulmonary and thoracic wall metastases (Fig. 5). They also showed a telangiectatic and hemangiopericytoma-like pattern. Considering these findings from the autopsy specimens, the final pathological diagnosis was giant cell-rich osteosarcoma.

Discussion

Osteosarcomas are composed of heterogeneous cell populations including giant cells. Whereas reports of giant cell-rich types are few because of histological similarity, it is often difficult to differentiate from benign or malignant GCT. Radiological findings including tumor location and histological characteristics such as anaplasia of stromal cells and osteoid formation can assist in making a definite diagnosis. However, clinical features are important to make the correct diagnosis.

In our case, the radiological finding presenting an osteolytic lesion that was typical of a giant cell tumor. As we mentioned above, recurrence was noted only a couple of months after initial surgical treatment because curettage was performed alone. Expecting local control, we tried wide resection with reconstruction of the wrist using a vascularized fibular autograft. However, several months after the second surgery, roentgenography showed soft part swelling suggesting local recurrence again. Locally aggressive disease and multiple recurrences appear to be risk factors for pulmonary metastases in benign giant cell tumor of bone. Further, local recurrence and the primary lesion at the distal radius seem to be associated with an increased risk of lung metastases. Patients of a giant cell tumor with lung metastases had favorable prognosis independent on the type of treatment used because spontaneous regression was reported. However, we initiated chemotherapy using pirarubicin, ifosfamide, and carboplatin because we suspected that this aggressive radiological finding might show a
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malignant bone tumor such as osteosarcoma. However, when we consulted pathologists about pathological features of operation specimens, they replied consistently that the features were characteristic of a conventional giant cell tumor, not osteosarcoma or malignant giant cell tumor. In spite of the intensive chemotherapy and radiation therapy, the patient died of progressive metastases. Autopsy revealed that pathological features from the metastatic lesions showing tumorous osteoid formation were similar to those of osteosarcoma, not giant cell tumor. Malignant transformation of giant cell tumor is less likely because the malignant transformation of the formerly conventional lesion should take many years without prior history such as local irradiation. It is rare to find patients younger than age 20 with malignant transformation. Differential diagnosis between giant cell-rich osteosarcoma and benign and malignant giant cell tumor is controversial even though histological findings such as tumor osteoid formation and anaplasia of the osteoclast-like giant cells were reported to be important for the diagnosis of osteosarcoma. Malignant giant cell tumor never produces tumor osteoid, bone, or cartilage in the manner that an osteosarcoma does. Bizarre giant cell forms are found with osteosarcoma, but the anaplastic nuclei are usually multilobulated, unlike the multinucleated osteoclast-like giant cells that characterize malignant giant cell tumors. Clinical features of the tumor location such as metaphyseal or diaphyseal centering and the existence of radiographic Codman’s triangle, intralesional fluffs, cortical ballooning, and faint onion-skin-like periosteal reaction also aid osteosarcoma diagnosis. Malignant giant cell tumor usually occurs in patients of advanced age, i.e., over 60 years, whereas most conventional giant cell tumors occur in patients of 20–50 years old. This case reports a seventeen-year-old patient. The tumor located in the epimetaphysis to epiphysis. Cortical ballooning was seen radiographically, although small Codman’s triangle and intralesional fluffs were apparent. Tumor osseous tissue production could be seen in metastatic lesions. Radiation-induced sarcomatous change can be excluded because of the short duration after radiation therapy and occurrence out of the irradiated areas. Based on these findings, the final diagnosis was a giant-cell-rich osteosarcoma.

Clinical features of the case provide clues to differentiating giant cell-rich osteosarcoma from the giant cell tumor of bone, a relatively common neoplasm occurring in the epiphyseal regions of patients of 20–40 years. When we meet patients presenting with giant cell tumor in terms of radiological and histological findings, especially when they are younger than the age at which giant cell tumor usually occurs, we should bear in mind giant cell-rich osteosarcoma and perform intensive chemotherapy and surgery.

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