Unusual Osteoblastic Secondary Lesion as Predominant Metastatic Disease Spread in Two Cases of Uterine Leiomyosarcoma

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Key Words

Uterine smooth muscle neoplasm · Leiomyosarcoma · Osteoblastic bone metastases

Abstract

Uterine smooth muscle tumors range from benign leiomyomata to low- and high-grade leiomyosarcomas. A leiomyosarcoma is a rare malignant smooth muscle tumor that infrequently metastasizes to the bone. In fact, initial presentation or recurrence as osseous metastases is extremely uncommon in patients with a history of leiomyosarcoma. On imaging, these bone lesions generally appear as lytic foci. The authors report here two cases of osteoblastic bone lesions in leiomyosarcoma of the uterus with predominant metastatic lesions localized in the bone.

Case Report

Case 1

In a 52-year-old woman, presenting with vaginal bleeding, a pelvic lesion of 6 × 6 × 5 cm was detected during a gynecological examination and on pelvic ultrasonography. The patient underwent total hysterectomy with bilateral salpingo-oophorectomy in April 2002. The pathological diagnosis was leiomyoma with a high mitotic index (>5/10 HPF), FIGO stage I. The margins of the mass were well-defined and the tissue immunostained positive for desmin. Tumor cells were arranged in fascicles and showed no coagulative cell necrosis or hemorrhage ([fig. 1](#)).

The patient received no further treatment after surgery, remaining without evidence of recurrence for the following 41 months. In September 2005, after experiencing symptomatic pain localized to the lumbar spine, the patient was examined using computed tomography (CT). The CT scan revealed

osteoblastic bone lesions localized on the sacrum, the left ischiopubic ramus, and the D7 vertebral body. A subsequent MRI scan, aiming at a more detailed evaluation of the spinal cord, confirmed the integrity of the D7 posterior cortex. A radionuclide bone scan revealed no radionuclide bone uptake, and a positron emission tomography (PET) showed activity only in a single nodule of 2.5 cm (SUV = 4.6) localized on the left pleural wall without other FDG-avid lesions.

The pleural nodule was excised and analyzed, revealing a recurrence of the primary tumor. Consequently, from October 2005 to February 2006, the patient was started on a chemotherapeutic treatment consisting of six cycles of 60 mg/m² epidoxorubicin on day 1 and 2 plus 1.8 g/m² ifosfamide on days 1 through 5 of a 21-day cycle. At the end of the treatment, CT showed an unchanged pattern of disseminations of bone lesions. A bone scan in September 2007 documented progression of the disease on D7 and new multiple bone metastases localized to the left humerus, D4, D5, D6, D8 vertebral body. CT showed a modified imaging of bone metastasis in all skeletal locations with mixed osteoblastic and lytic patterns. The patient underwent radiation of the spinal lesions with a total administration of 20 Gy. At the end of the radiotherapeutic treatment, she was treated with six cycles of a 75-mg/m² Taxotere q3w monochemotherapy (from October 2007 to April 2008). In August 2008, CT showed an increase of the osteoblastic pattern of the D7 vertebral body and new bone lesions localized in the right hip and femur bone. Consequently, radiotherapy at a total dose of 16 Gy was administered to the new lesions area. After two months the disease showed further bone progression and the patient refused any further treatment.

Case 2

A 68-year-old woman, with a medical history of pelvic pain and bladder discomfort, was referred for a gynecological examination in November 2005.

Pelvic ultrasonography revealed a large solid pelvic mass, measuring 17 × 15 × 11 cm. The patient therefore underwent surgery consisting of hysterectomy and bilateral salpingo-oophorectomy in December 2005. Histopathological diagnosis indicated that the excised mass was a myxoid leiomyosarcoma: mitotic index 20/10 HPF, FIGO stage I. Histological evaluation of the specimens revealed elongated leiomyosarcoma cells with a high mitotic index, abundant cytoplasm and cigar-shaped nuclei with subnuclear vacuoles ([fig. 2](#)).

From January to May 2006, four cycles of adjuvant chemotherapy were administered consisting of 60 mg/m² epidoxorubicin on day 1 and 2 and 1.8 g/m² ifosfamide on days 1 through 5 q3w. On March 2007, CT showed a pelvic mass of 7 cm, while PET detected an increased uptake localized on the L5–S1 vertebral body that was classified as a marker of degenerative skeletal change. Bone scan was negative. The patient underwent surgery to remove the pelvic mass. Histopathology of the mass confirmed that it was indeed a recurrence of the primary tumor.

After surgery, pelvic radiotherapy was administered at a total dose of 50 Gy in August 2007. In June 2008, the patient presented with sudden pain localized to the sacrum. MRI and CT revealed the presence of osteoblastic bone lesions localized to the sacrum and the left hip and a pelvic mass of 3 cm. These findings were confirmed by PET and bone scan. Consequently, chemotherapy with docetaxel (75 mg/m² on day 1) and gemcitabine (1,000 mg/m² on days 1 and 8) every 21 days, was administered for three cycles. At the end of this treatment, CT showed an increase of the pelvic mass but no change in the number of dissemination points and in the morphology of osteoblastic bone lesions.

A third-line chemotherapy with paclitaxel at a dose of 175 mg/m² associated with carboplatin AUC 5 q3w was administered for three further cycles. At completion of the last cycle of chemotherapy, the progression of both pelvic mass and of osteoblastic bone metastasis was documented with CT. From this point in time only supportive therapy was administered when needed.

Discussion

Uterine leiomyosarcoma accounts for approximately 1% of all uterine malignancies [1, 2]. Distant metastasis is generally a late manifestation of leiomyosarcomas and most commonly occurs in the lung, liver, kidney, and brain [3]. Bone metastatic lesions caused by leiomyosarcoma are rare and generally appear as osteolytic lesions. Reviewing the literature, we were able to find few cases of leiomyosarcoma recurrence occurring in bone.

Elhammady et al. [4] recently reported a case of spinal osteoblastic bone metastasis as the presenting symptom of leiomyosarcoma recurrence and reviewed six cases of leiomyosarcoma initially presented as spinal metastases. Shapiro et al. [5] described a case of uterine smooth muscle tumor of uncertain malignant potential that recurred as a high-grade leiomyosarcoma in the humerus, 5 years after its successful removal by hysterectomy.

Early diagnosis of bone metastases was difficult in both cases reported. In the first case, CT and MRI demonstrated higher sensitivity than PET and bone scan in detecting osteoblastic metastases. In the second case, PET was effective in detecting bone metastasis although the diagnosis of osteoblastic secondary lesion was confirmed only one year later by MRI. Usually bone scan seems to be superior to PET in detecting osteoblastic metastases, while MRI appears more reliable than PET in patients with PET-negative tumors [6].

Despite the poor response to chemotherapy observed in our two cases, the course of the disease was more indolent than in cases with prevalent extensive visceral metastases.

Although leiomyosarcoma infrequently metastasizes to the bone, the two cases we reported showed unusual predominant patterns of osteoblastic disease recurrence. Therefore, a diagnosis is recommended only after careful evaluation of the results obtained by all available radiological techniques.

Fig. 1. **a** Smooth muscle tumor cells arranged in fascicles. **b** Immunostaining positive for desmin.

Fig. 2. **a** Histologically stained leiomyosarcoma cells with cigar-shaped nuclei and eosinophilic cytoplasm. **b** Neoplastic cells with several mitotic figures (original magnification 60 × HE)

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