Bone metastasis as a presenting feature of endometrial adenocarcinoma: case report and literature review

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Summary

A rare case of endometrial adenocarcinoma that presented with symptoms of bone metastasis in the right ischium is described. The patient had no signs or symptoms of gynecological malignancy and the diagnostic work up did not reveal the primary disease. The bone metastasis was treated successfully by radiotherapy, but three years later the patient noted vaginal bleeding, which led to the diagnosis and treatment of the primary endometrial cancer. Another 20 cases of endometrial carcinoma with bone metastasis have been found in literature, but only five of them presented with the feature of bone metastasis. Bone metastasis should be considered in patients with endometrial adenocarcinoma.

Key words: Endometrial adenocarcinoma; Bone metastasis.

Introduction

Endometrial carcinoma is the most common malignancy of the female genital tract. The disease is usually diagnosed in early stage and has a good prognosis. Abnormal vaginal bleeding is the presenting symptom in 90% of cases and leads to early diagnosis [1]. Approximately 78% of endometrial cancers are FIGO Stage I with a five-year survival of 90% [2].

Metastasis of endometrial cancer to bone is very uncommon and usually is diagnosed in patients with advanced disease [3]. There are only a few cases of endometrial carcinoma presenting with bone metastasis in the literature. We report a case of endometrial cancer that presented with pelvic bone metastasis, while the primary disease was diagnosed three years later.

Case Report

A 68-year-old woman, gravida 3, para 3, presented in 2001 with right hip pain, which had started three to four months earlier. X-rays of the right hip revealed a lytic lesion of the pelvic bone. A computed-tomography (CT)-guided needle biopsy from the lytic lesion at the right ischium revealed well differentiated metastatic adenocarcinoma of unknown primary.

The patient had no other bone pain. There were no gynecological complaints, no postmenopausal vaginal bleeding, spotting or discharge and she had no constitutional symptoms. A recent (6 months before) Papanicolaou smear was normal. A diagnostic workup was initiated and included a bone scan which revealed intense uptake only at the right ischiatic ramus of the pelvis and associated tissues. CT of the lungs and abdomen revealed no other pathology. Mammography, pyelography, ultrasonography of the thyroid gland and intenstine radiography showed no suspicious lesions. Magnetic resonance imaging (MRI) was also suggestive of a bone tumor but no other abdomen pathology. Laboratory studies, including a hematology profile, serum chemistries, urinalysis, thyroid studies, CA125 and carcinoembryonic antigen (CEA) were normal.

During the diagnostic workup, the patient suffered deep vein thrombosis (DVT) of her left leg (involving the popliteal and posterior tibialis veins), which was successfully managed by thrombolytic agents.

Consequently since no primary site of adenocarcinoma was detected the patient received radiotherapy (3000 cGy in 10 fractions). Pain relief was achieved and the patient was monitored in a follow-up program.

Three years later radiography demonstrated healed bone and the patient remained in complete clinical remission, but reported abnormal vaginal bleeding. She underwent endometrial cutterage and a well differentiated endometrioid adenocarcinoma was diagnosed. Subsequently, she underwent a total hysterectomy, bilateral salpingo-oophorectomy, and bilateral pelvic lymphadenectomy; biopsies of the omentum and peritoneum were also obtained. A small lesion, less than 1 cm in diameter, was noticed and excised from the rectus. No other gross intraabdominal abnormalities were noted at laparotomy, and peritoneal lavage was obtained prior to hysterectomy.

Cytology of peritoneal lavage did not detect any malignancy. Histopathology of the uterus revealed extensive well differentiated endometrioid carcinoma extending from the fundus to the lower uterine segment, and to the anterior half of the endocervix with stromal invasion. The tumor infiltrated more than two-thirds of the myometrium and there were areas suggestive of lymphatic invasion. The same carcinoma was diagnosed in the specimen from the rectus. The ovaries, lymph nodes, omentum and peritoneal biopsies were negative. The patient was diagnosed as FIGO Stage IV A Grade 1.

Postoperatively the patient received adjuvant chemotherapy consisting of andriamycine 50 mg/m^2 and cisplatinum 75 mg/m^2 for four cycles. Considering that the tumor was well differentiated and therefore hormonally responsive, the patient was given 160 mg of megestrol acetate daily as maintenance therapy. One year later the patient was disease-free with no activity limitations and with a normal abdomen CT, mammogram and pap smear.

Radiography of the pelvis was without evidence of persistence or recurrence of the tumor.

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Discussion

The prevalence of bone metastasis from endometrial cancer is very low, varying from 2-8% [4]. However, Abdul-Karim *et al.* in a retrospective study including bone metastasis from endometrial cancer detected both clinically and at autopsy reported the highest incidence, 25% [3]. In another large clinical study of 927 patients with endometrial carcinoma, only 47 (4.8%) were found to have Stage IV disease and only two (0.05%) had bone metastasis [5].

In the literature, we found only 20 reported cases with bone metastasis (Table 1). In five cases the bone metastasis represented the presenting manifestation of the disease. In the others the interval between the detection of endometrial cancer and bone metastasis varied from six months to five years (mean 3 years) [5].

Bone metastases are rare and often seen together with abdominopelvic recurrences and/or other organ metastases, such as lung, kidney and liver. Because metastatic bone disease in endometrial carcinoma is rare, the presence of a second primary malignancy such as carcinoma of the breast, lung, kidney, bladder or thyroid grand must be considered. The routine clinical evaluation should include CT scans of the lungs and abdomen and also mammography, ultrasound scan of the thyroid gland and cystoscopy.

Endometrial carcinoma spreads by different mechanisms. Contiguous invasion from the endometrial surface into the endocervix or fallopian tube or direct myometrial penetration is common. Lymph node metastases via Batson's plexus and the systemic vertebral plexus to the vertebrae and pelvic bones are usual. The mechanism by which this tumor metastasizes to distal sites remains unclear. Invasion of the blood vessels by the tumor could suggest a hematogenous route of spread to explain distal metastases to the lung, bone and other sites.

Trauma, temperature differences, hormonal factors, local hemodynamic influences and host immune response have also been implicated as determiments of the site of tumor emboli seeding [24].

In the study of Abdul-Karim *et al.*, bone metastasis occurred only in high-grade carcinomas but in the case we report and in other reported cases it occurred in low-grade disease which explains the long disease-free period and good survival in such cases [11]. In general, the prognosis is poor and the average time from radiographic documentation of skeletal involvement at any site to death is 6.6 months [2]. Since only a few patients with endometrial cancer and bone metastases have been reported, there is not enough evidence about the prognosis of the disease.

The treatment of these patients includes surgical management of the endometrial cancer, radiotherapy and hormonal therapy when indicated. Radiation is very effective in the management of bone metastasis and palliative chemotherapy can improve survival.

An interesting aspect about our patient is that the diagnosis of endometrial cancer was established three years after the presentation of bone metastasis. This was because the patient had no clinical signs or symptoms to suggest gynecological malignancy, a recent pap smear was normal and, also the CT and ultrasound of the abdomen did not reveal any pathology to indicate endometrial biopsy. It should also be noted that it was a very rare case since only five patients with endometrial cancer presenting with future bone metastasis have been reported in the literature.

Table 1. — *Clinicopathologic features of patients with endometrial cancer and bone metastasis.*

Author/year	Age	FIGO stage	Bone metastasis as the presenting manifestation	Site of bone metastasis	Other metastasis Recurrence
Vaneck *et al.* [6] 1967	67	I	–	R fibula	No
(2 cases)	54	IV B	–	L fibula	No
Janis *et al.* [7] 1976	?	II	–	L calcaneus	No
Beller *et al.* [8] 1982	59	I C G_2	–	L femur	No
Onuba *et al.* [4] 1983	57	IV B G_3	–	R tibia	Lung, Kidney
Litton *et al.* [9] 1991	55	I B	–	R calcaneus	No
Nishida *et al.* [10] 1994	61	III B G_1	–	L calcaneus	No
Cooper *et al.* [11] 1995	59	IV G_2	+	R calcaneus	No
Schools *et al.* [12] 1995	66	I A G_3	–	R humerus	No
Petrun *et al.* [13] 1995	61	IV B G_1	+	L tarsus	No
Clark *et al.* [14] 1996	55	IV B	–	R calcaneus R talus	Lungs
Malicky *et al.* [15] 1997	44	IV B G_2	+	L femur	No
Armentano *et al.* [16]* 1997	74	I A*	–	L tibia	No
Dosoretz *et al.* [17] 1999	71	IV A G_3	–	L mandible	No
Rocha *et al.* [18] 2000	67	IV B	–	L mandible	Lung, Kidney
Sahinler *et al.* [19] 2001	67	I C G_3	–	Bilat. tibia, bilat. femur, metatarsal bones	Vaginal reccurence
Mustafa *et al.* [20] 2001	45	IA G_2	–	Cranial bone	Liver, Lung abdominal recurrence
Neto *et al.* [21] 2002	39	IV B G_2	+	R ischium	No
Manolitsas *et al.* [22] 2002	76	IV B G_3	+	R calcaneus	No
Wimhurst *et al.* [23] 2003	77	I C G_3	–	L metatarsal bones	Lungs
Giannakopoulos 2005	68	IV A G_1	+	R ischium	No

*Coexistent squamous cell carcinoma of the cervix.

Bone metastases may be seen in endometrial cancers and in some cases these metastases cause the presenting symptoms of the disease.

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