An extremely rare presentation of relapse in endometrioid endometrial adenocarcinoma: isolated metastases to the tibia and humerus. Case report and review of the literature

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Summary

In endometrial carcinoma patients, metastases to bones are rare and isolated metastases to extremities are extremely rare. We describe the case of a 59-year-old patient who underwent surgery followed by adjuvant radiotherapy due to endometrioid endometrial adenocarcinoma (grade 2, FIGO Stage II). After intervals of nine and 18 months respectively, she was diagnosed with metastatic tumours located in the right tibia and in the left humerus. The metastases were confirmed by biopsy. Following irradiation of metastatic lesions, the relief of symptoms was observed, and the patient remains under observation. We conclude that patients presenting a history of endometrial carcinoma with chronic pain in the extremities should be carefully evaluated, because although extremely rare, the carcinoma can metastasize to bones. Treatment of bone metastasis from endometrioid endometrial carcinoma by irradiation may increase quality of life and prolong survival.

Key words: Endometrial carcinoma; Endometrioid; Relapse; Bone extremities.

Introduction

Endometrial carcinoma is the most common invasive neoplasm of the female genital tract and accounts for 7% of all invasive cancer in women. The majority of patients are diagnosed with no evidence of extrauterine spread (70-80% Stage I), which gives patients a better prognosis [1]. In more advanced disease the sites commonly affected outside the uterus are the pelvic and paraaortic lymph nodes and ovaries [2]. Distant metastases in advanced or recurrent endometrial cancer most commonly involve the lungs, liver, central nervous system and skin [2, 3]. Metastases to bones have been described only in 2-15% of patients with recurrent disease [2, 4]. In such cases, the primary tumour is usually poorly differentiated (G3), of a high stage, and indicative of recurrent disease [5]. Metastatic tumours are usually seen together with abdominopelvic recurrences and/or other organ metastases and generally are located in the axial skeleton. The most common site of osseous metastases are vertebrae, with pelvic bones, ribs and sternum being less common sites [1, 4-6]. Metastases to extremities are extremely rare and thought to result from the haematological spread of carcinoma cells [3, 5].

A review of the English literature indexed in Medline was done. By searching the items endometrial carcinoma and metastases to extremities 20 such cases were found [1-19]: 11 cases of single osseous relapses of endometrial carcinoma in the extremities (Table 1) and nine cases when metastatic tumour of the foot was the first manifestation of endometrial carcinoma (Table 2). Although local recurrences of endometrial carcinoma often occur early with evident symptoms, development of metastatic disease to the bones may cause difficulties in a prompt diagnosis.

Case Report

A 59-year-old patient presented with postmenopausal vaginal bleeding. Computed tomography (CT) scans showed an enlarged uterus and no other suspicious abdominopelvic lesions. An endometrial biopsy confirmed endometrial carcinoma. The patient was treated with total abdominal hysterectomy, bilateral salphingo-oophorectomy and pelvic lymph node dissection in January 2008. The histological diagnosis was a moderately differentiated (G2) endometrioid endometrial adenocarcinoma invading the outer half of the myometrium (> 1/2) with cervical stroma. However, the fallopian tubes and ovaries showed no signs of tumour invasion and the pelvic lymph nodes were negative. No evidence of abdominopelvic metastases was found at surgery. Her disease was classified as clinical Stage II according to FIGO 2009 staging and in the TNM classification it was pT2 N0 M0.

The patient was treated with external and intracavitary irradiation until April 2008. External pelvic irradiation was delivered to the pelvis by Co60 through four fields and a total dose of 44 Gy was given in 22 fractions. The intracavitary treatment was performed during the external irradiation using a high-dose-rate Co60 unit, with 18 Gy being delivered to the vaginal surface in three fractions.

The patient was disease-free and asymptomatic during the first six months after treatment. However in October 2008, pain and swelling of the right shin appeared. After a month, bone

Revised manuscript accepted for publication January 7, 2011

Table 1. — *Isolated metastasis to the bone extremities as the presentation of relapse in endometrial carcinoma patients – review of the literature*.

Author/year (references)	Age (years)	Histology	Stage/ Grade	Interval to relapse (months)	Bone involved	Other metastasis	Treatment	Survival (months)
Vanecko R.M., *et al.*/1967 [10]	67	–	I / –	–	fibula	–	–	–
Janis L.R., Feldman E.P./1976 [7]	–	endometrioid adenocarcinoma	II / –	36	calcaneus	No	radiotherapy	–
Beller, *et al.*/1982 [9]	59	–	I / –	–	femur	No	–	–
Litton G.J., *et al.*/1991 [13]	55	endometrioid adenocarcinoma	I / 2	24	calcaneus	No	radiotherapy	> 10
Nishida Y., *et al.*/1994 [11]	61	endometrioid adenocarcinoma	III / –	–	calcaneus	No	–	–
Schȍls W.A., *et al.*/1995 [14]	66	endometrioid adenocarcinoma	I / 3	18	humerus	No	radiotherapy, hormontherapy	> 24
Sahinler I., *et al.*/2001 [4]	67	endometrioid adenocarcinoma	I / 3	4	metatarsus	vagina	radiotherapy	2
Dursun P., *et al.*/2003 [5]	51	endometrioid adenocarcinoma	III / 3	2	humerus	lymph nodes	radiotherapy	6
Amiot R.A., *et al.*/2005 [2]	86	endometrioid adenocarcinoma	III /	18	hallux	pulmonary	surgery	> 1
Landoni F., *et al.*/2006 [8]	66	endometrioid adenocarcinoma	III / 2	19	calcaneus, cuboid bone	No	radiotherapy	–
Qin Y., *et al.*/2008 [12]	48	endometrioid adenocarcinoma	II / 3	22	bilateral femur	No	surgery, chemotherapy, radiotherapy, hormontherapy	> 42
This case, 2010	59	endometrioid	II / 2	9	tibia, humerus	No	radiotherapy	> 29

scintigraphy demonstrated hot spots in the right tibia and in the left humerus (Figure 1). A biopsy of the right shin tumour was taken, and metastatic carcinoma was confirmed (Figure 2). The patient underwent irradiation by Co60 up to a total dose of 8 Gy, and received chemotherapy AP1 (doxorubicin and cisplatinum). Treatment ended in April 2009 and relief of symptoms was observed.

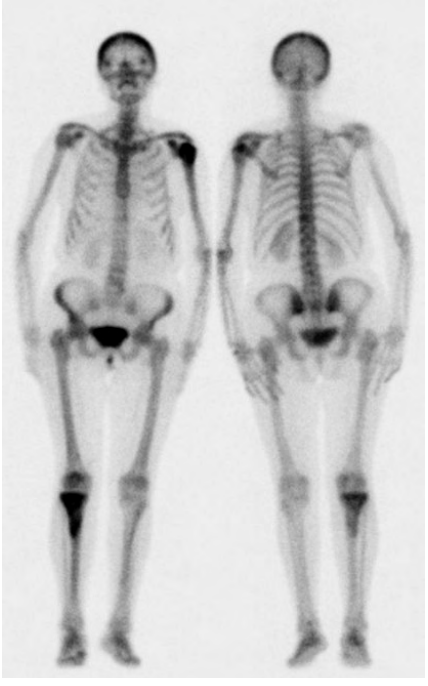

Figure 1. — Whole body bone scintigraphy demonstrating hot spots in the right tibia and the left humerus.

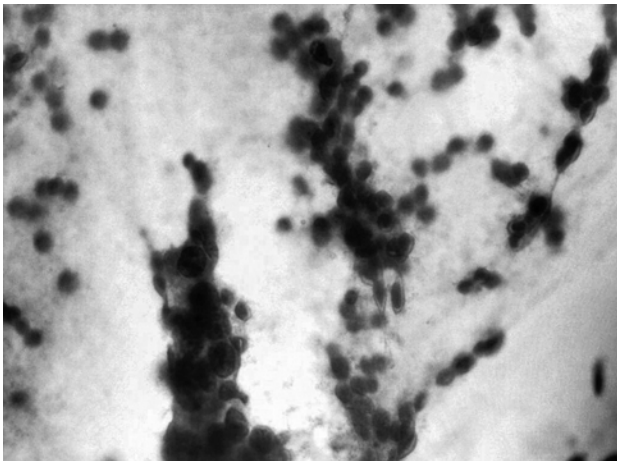

Figure 2. — Carcinoma cells in the fine needle aspiration of the metastatic tumour of the foot – (H+E, 200x magnification).

In June 2009 pain in the left arm appeared. The X-ray picture showed metastasis to the head of the left humerus (Figure 3), which was later confirmed by biopsy. After irradiation by Co60 until a total dose of 20 Gy, relief of symptoms was observed. However, in February 2010, pain and swelling returned – this time in the left arm. In CT, massive neoplastic infiltration was visualized involving the head of the humerus and the soft tissues of the left arm with regional nodal involvement. The patient was disqualified from surgery and treated by palliative irradiation by Co60 until a total dose of 20 Gy in the tumour area. The treatment was well tolerated, relief of symptoms was observed and the patient remains under observation. During observation from surgery from January 2008 to July 2010, no another locations of metastases were detected.

Table 2. — *Isolated metastasis to the bones of the extremities as the first manifestation of endometrial carcinoma – review of the literature.*

Author/year	Age (years)	Histology	Grade	Bone involved	Other metastasis	Treatment	Survival (months)
Vanecko R.M., *et al.*/1967 [10]	54	–	–	fibula	–	–	–
Onuba O./1983 [19]	57	endometrioid adenocarcinoma	–	tibia	lung, kidney	–	–
Cooper J.K., *et al.*/1994 [6]	59	endometrioid adenocarcinoma	2	calcaneus	No	chemotherapy, radiotherapy	> 60
Petru E., *et al.*/1995 [17]	61	endometrioid adenocarcinoma	1	tarsus	No	chemotherapy, hormontherapy	10
Malicky ES, *et al.*/1997 [18]	44	endometrioid adenocarcinoma	2	femur	No	radiotherapy, hormontherapy	> 12
Manolitsas T.P., *et al.*/2002 [1]	76	endometrioid adenocarcinoma	3	calcaneus	No	radiotherapy	20
Uharcek P., *et al.*/2006 [16]	67	endometrioid adenocarcinoma	1	calcaneus, talus and metatarsal bones	No	surgery, chemotherapy, hormontherapy	> 20
Loizzi V., *et al.*/2006 [3]	73	endometrioid adenocarcinoma	3	tibia	No	chemotherapy	9
Kaya A., *et al.*/2007 [15]	70	endometrioid adenocarcinoma	1	tibia	No	radiotherapy	> 47

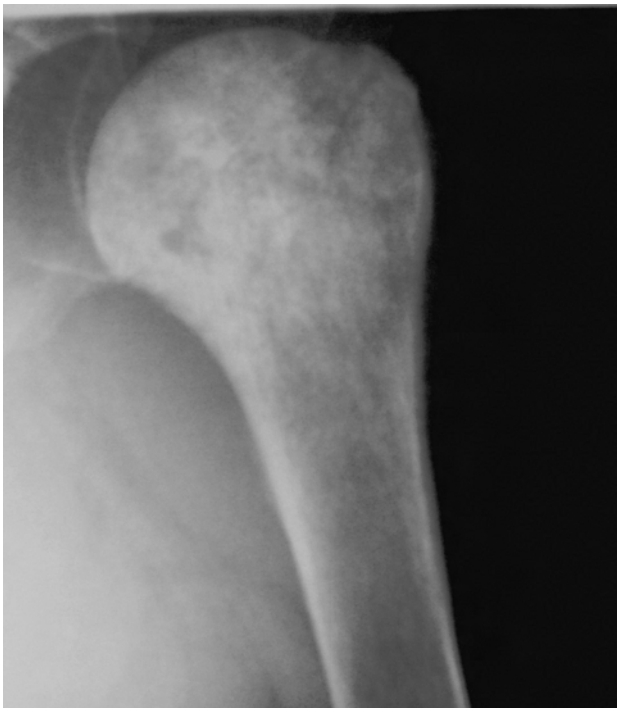

Figure 3. — Radiograph of the left humerus demonstrating osseous destruction in bone metastasis of endometrioid endometrial adenocarcinoma.

Discussion

In patients with female genital tract carcinomas, despite the rarity of metastases to the extremities, clinicians must have a high index of suspicion for metastasis in patients with a history of carcinoma who present with swelling or bony tenderness [2, 4, 5, 7-14]. Since symptoms may mimic other benign conditions, it is important to consider bone metastasis as a possible diagnosis in patients with osseous pain which does not respond to conservative treatment [9, 10]. Appropriate imaging of suspected bone extremity metastases may include plain X-rays and radionuclide bone scans [1]. Technetium biphosphonate bone scans are extremely useful and can be positive up to 18 months before a lesion is detectable on a plain X-ray image [13]. Therefore, a biopsy should be performed in patients with suspected lesions, and who demonstrate evidence of bony destruction [2]. In the case of a confirmed isolated metastatic lesion in a bone extremity, treatment by irradiation, with or without surgery, hormones and chemotherapy, is reported as effective in most cases, and may be curative [2, 3, 6, 10, 12, 13, 15-19].

The case report presented in the previous section has three main peculiar features: 1) it demonstrates an endometrial carcinoma presenting with an osseous metastasis, which is a rare occurrence, 2) the metastatic tumours were located in the extremities, which is extremely rare, 3) the bone lesions were single bone metastases, which again, is unusual in such cases. Additionally, the case is not only the first known to us of an isolated relapse of endometrial carcinoma in the tibia but also the third case of isolated relapse of the carcinoma in the humerus (Table 1) [5,13].

Finally, patients with chronic pain in the extremities and who demonstrate evidence of bone destruction, especially presenting a history of endometrial carcinoma, should be carefully evaluated because although extremely rare, it is possible for the carcinoma to metastasize to bones. Treatment of bone metastasis from endometrioid endometrial carcinoma by irradiation may increase quality of life and prolong survival.

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