Bilateral femur metastasis in endometrial adenocarcinoma

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ABSTRACT

يعتبر انتشار الورم الغدي السرطاني في العظم أمراً غير شائع، ويعتبر انتشاره في عظم الفخذ على الجانبين نادراً للغاية. خضعت امرأة تبلغ من العمر ٤٨ عاماً وهي مصابة بورم غدي سرطاني في بطانة الرحم من المرحلة الثانية الدرجة ٢–٣ حسب (FIGO) (الاتحاد الدولي لأمراض النساء والولادة) لعملية استئصال الرحم الإشعاعي العلاجي. أجريت لها عملية استئصال الغدد اللمفية على الجانبين من البوق والمبيضين والحوض وبجانب الأورطي، عقب ذلك خضعت للعلاج الإشعاعي والعلاج الكيميائي. بعد اثنان وعشرين شهراً من العملية الجراحية، كانت المريضة تعاني من ألم متزايد، ثم حضرت إلى المستشفى وهي تعاني من انتشار للمرض في عظم الفخذ على الجانبين. تمت معالجتها بالاستئصال الجراحي الجزئي لانتشار المرض في العظم وبالعلاج المساعد بما في ذلك العلاج الكيميائي والعلاج الإشعاعي الملطف والعلاج الهرموني. بعد مرور ثلاث سنوات ونصف من علاج الانتشار في العظم، بقيت المريضة في وضح جيد من الناحية السريرية. قد يظهر انتشار الورم الغدي السرطاني لبطانة الرحم في العظم في بعض المواقع غير العادية وينبغي أخذ انتشار المرض في عظم الفخذ على الجانبين بعين الاعتبار لدى المرضى. عادة ما تقاوم العلاجات متعددة النماذج من انتشار الورم الغدي السرطاني لبطانة الرحم في العظم.

Bone metastasis of endometrial carcinoma is uncommon, and bilateral femur metastasis is extremely rare. A 48-year-old woman with Federation International of Gynecology and Obstetrics stage IIB grade 2-3 endometrial adenocarcinoma underwent curative radical hysterectomy, bilateral salpingo-oophorectomy, and pelvic and para-aortic lymphadenectomy followed by radiotherapy and chemotherapy. Twenty-two months after surgery, she suffered from progressive pain and then presented bilateral femur metastasis. She was administered the surgical excision of bony metastasis and adjuvant therapies including chemotherapy, palliative radiation, and hormone therapy. Three and a half years after treatment of bony metastasis, she remains clinically well. Bone metastasis of endometrial carcinoma may occur at some unusual sites, and bilateral femur metastasis should be considered in patients. Multimodal therapies are usually advocated for bone metastasis of endometrial carcinoma.

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Endometrial carcinoma is one of the most common gynecological malignancies that has a good prognosis. However, the local recurrences and distant metastasis continue to be a big problem in high-risk patients. Bone metastasis in endometrial carcinoma is less common than those to the lung and liver, and it is thought to result from hematogenous spread. The femur metastasis of endometrial carcinoma is a rare situation, but it should be considered in patients. In this paper, to highlight the situation, we report a case of a 48-year-old woman (ethically approved by the patient) with Federation International of Gynecology and Obstetrics (FIGO) stage IIB grade 2-3 endometrial carcinoma who presented with bilateral femur metastasis 22 months after primary surgery, and reviewed related available literature using the Medline search.

Case Report. A 48-year-old woman presented with complaints of postmenopausal bleeding in October 2001. She had ceased menstruation at the age of 45, and she was in apparent good health until February, 2001, when she began to have abnormal bleeding. Fractional dilatation and curettage were performed and histopathology revealed endometrial adenocarcinoma

Figure 1 - X-ray shows bone destruction of the bilateral proximal femurs.

Figure 2 - Computer tomography scan shows osteolytic lesions of both femurs.

with cervical involvement. Radical hysterectomy, bilateral salpingo-oophorectomy, and bilateral pelvic and para-aortic lymphadenectomy were carried out in October 2001. The pathology demonstrated a moderately to poorly differentiated endometrial adenocarcinoma with invasion to cervix, and the full-thickness of myometrium and lymph vascular space were involved. Other sites, including vaginal, adnexa, all the lymph nodes and the surgical margins were negative. Peritoneal cytology was also negative. The final diagnosis was FIGO stage IIB (G2-3) endometrial adenocarcinoma. Postoperative chemotherapy was given for 6 cycles consisting of cisplatin 50 mg/m^2, Adriamycin 50 mg/m^2, and cyclophosphamide 500 mg/m^2. She also underwent adjuvant postoperative irradiation therapy radiotherapy with a total dose of 26GY for intracavitary radiation and a total dose of 40GY for whole pelvis external beam therapy. Twenty-two months after primary surgery, she presented with right hip pain without any swelling and redness. Eight months later she was admitted to hospital because of progressive pain. Osteolytic lesions located in the neck and greater trochanter of both femurs were detected by x-ray and computer tomography (CT) scans (**Figures 1 & 2**), suggestive of metastatic lesion. In May 2004, she underwent surgical excision of bony metastasis of both femurs with bone cement padding and she also underwent internal fixation with DHS (dynamic hip screw) for the right hip. The pathological result confirmed metastatic endometrial adenocarcinoma of bilateral femur with moderate differentiation. The estrogen and progesterone receptors were all positive. Meanwhile, chest CT scan showed multiple nodules in both the upper right and left lobes, which suggested metastatic lung tumor. After surgery she was administered adjuvant chemotherapy for 6 cycles consisting of cisplatin 50 mg/m^2, Adriamycin 50 mg/m^2, and cyclophosphamide 500 mg/m^2. Palliative radiotherapy with a total dose of 40GY was given to relieve the hip pain. At the same time, hormone therapy was initiated. On follow-up, the bilateral mammography, pelvic examination, pap smear, x-rays, CT scans, and the whole-bone scanning of the patient all showed no evidence of persistence or recurrence of the tumor. Three and a half years after the treatment of the femoral metastasis, she remains clinically well.

Discussion. The incidence of bone metastasis in endometrial carcinoma is low, ranging from 1-8% in the previous literature.[1-3] Abdul-Karim et al[4] reported 25% bone metastasis of endometrial carcinoma through autopsy, which accounts for the highest incidence to date. The most common site of bone metastasis of endometrial carcinoma is the vertebrae, whereas the appendicular skeleton metastasis is only approximately 1%.[3,4] Femur involvement of endometrial carcinoma is extremely rare. The interval from primary diagnosis to detecting bone metastasis is 2-3 years on average.[1,5,6] Endometrial carcinoma usually spreads to the vertebrae and pelvic bones via the Batson's plexus and the vertebral valveless venous plexus, and the spread to the limbs is thought to be hematogenous.[6,7] The lower extremity bones invasion may be explained by venous retrograde flow of tumor emboli to the leg.[6,8]

On literature review, we only have found 5 reports on femoral metastases of endometrial carcinoma. In 1990, Abdul-Karim et al[4] studied 67 patients with primary endometrial carcinoma through autopsy and found 2 of them presented femoral metastasis (no further details were presented). The other 4 were reported by Brufman et al[7] in 1978, Beller et al[5] in 1982, Malicky et al[3] in 1997 and Dursun et al[9] in 2006. The details of the last 4 cases as well as ours are shown in **Table 1**.

Table 1 - Femoral metastasis of endometrial carcinoma: review of the literature.

Author and publication year	Age (years)	FIGO stage	Primary tumor type/grade	Therapy for primary tumor	Clinical presentation of metastasis	Metastatic site of femur	Time between primary surgery to detecting bone metastasis	Therapy for femur metastasis	Post bone metastatic survival
Brufman et al,[7] 1978	69	-	Adenocarcinoma/*	Radiation and hormonal therapy	A painful mass	Right minor trochanter	Both were found at the same time	Radiation and hormonal therapy	>1.5 years
Beller et al, [5] 1982	59	I	Adenocarcinoma/ G2	Surgery (RAH/ BSO/PLND)	Swelling, and progressive pain	Lower shaft of left femur	9 months	Radiation, chemotherapy (doxorubicin-cyclophosphamide) and hormonal therapy (megace)	Not reported
Malicky et al,[3] 1997	44	IVB	Adenocarcinoma/ G2	Surgery (TAH/ BSO/PLND), chemotherapy and hormonal therapy	Progressive pain	Proximal femoral metaphysic and greater trochanter of left femur	Both were found at the same time	Radiation, chemotherapy (cisplatin and Adriamycin) and hormonal therapy (megestrol)	>2 years
Dursun et al,[9] 2006	69	IIIC	Endometrial clear cell carcinoma/G3	Surgery (TAH/ BSO/PLND/ PAND/IO)	Increased back and hip pain	Collum of the right femur and trochanter major of the left femur	3 weeks	Chemotherapy (Carboplatin and Taxol)	Within 1 month
Present report	48	IIB	Adenocarcinoma /G2-3	Surgery (RAH/ BSO/PLND), chemotherapy and radiation	Progressive pain	Neck and greater trochanter of bilateral femurs	30 months	Radiation, chemotherapy and hormonal therapy	>3.5 years

* - Information not provided by the authors, TAH - total abdominal hysterectomy, RAH - radical abdominal hysterectomy, BSO - bilateral salpingo-oophorectomy, PLND - pelvic lymph node dissection, PAND - para-aortic lymph node dissection, IO - infracolic omentectomy

The diagnosis of femur metastasis can be challenging, as the symptoms of pain and swelling are usually attributed to other more common diseases such as inflammation, arthritis, trauma, and so forth.[10] On literature review, all the reported cases including our case had the only complaints of progressive pain and swelling for femoral metastasis. There are several imaging techniques including plain x-rays, CT, and magnetic resonance imaging that can be used to determine bone metastases, but whole-radionuclide bone scanning is regarded as the most reliable and sensitive method for detection and extension of the bone metastasis.[9] A combination of systemic chemotherapy, local radiotherapy, and hormonal therapy might be effective in patients with bone metastases of endometrial carcinoma. It is reported that the one-year and 3-year survival for patients with distant recurrent disease of endometrial carcinoma are 39.2% and 14.2%.[2] The average survival from radiographic documentation of bone metastasis to death in endometrial cancer patients is 6.6 months.[4] In the previous reports as well as ours, most patients were administered the multimodal therapies including radiation, chemotherapy, and hormonal therapy for bone metastasis. The survival after bone metastasis was more than 1.5 years, except the latest case with multiple-bone involvement, which has the survival within one month. For the present case, the patient has had a 3.5-year progression-free survival after multimodal treatment of bony metastasis and remains clinically well now.

In conclusion, bone metastasis of endometrial carcinoma may occur at some unusual sites and femur metastasis should be considered in patients. As there are very few reports regarding the therapies for bone metastasis of endometrial carcinoma, we cannot propose the optimal mode of treatment for bone metastasis. However, multimodal therapies including systemic chemotherapy, palliative radiation, as well as hormonal therapy, are usually advocated.

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