Isolated Bone Metastases in Early Stage Endometrial Adenocarcinoma: A Case Report and Review of the Literature

Mevlut KURT1, Saadettin KILICKAP2, Sercan AKSOY2, Mustafa ERMAN2, Gokhan GEDIKOGLU3, Alev TURKER2

1 Turkiye Yuksek Ihtisas Teaching and Research Hospital, Department of Gastroenterology
2 Hacettepe University Institute of Oncology, Department of Medical Oncology
3 Hacettepe University Faculty of Medicine, Department of Pathology, Ankara, TURKEY

ABSTRACT
Isolated skeletal metastasis of endometrial carcinoma is very unusual. Herein, we report a 62-year-old woman diagnosed as FIGO stage IC, grade I, endometrial carcinoma who was found to have isolated femur and tibia metastases just after completing local radiotherapy. Incisional biopsy revealed metastatic adenocarcinoma. Following radiotherapy, medroxyprogesterone acetate and zoledronic acid was given. After a month, spontaneous right proximal femur fracture occurred and new bone metastasis was detected. Local radiotherapy and six cycles of paclitaxel and carboplatin were given; however, during a 3-year follow-up, bone metastases progressed. We review the endometrial carcinoma with bone metastasis in literature.

Keywords: Endometrial carcinoma, Bone metastasis, Treatment

ÖZET
Erken Evre Endometrium Adenokanserinde İzole Kemik Metastazları: Olgu Sunumu ve Literatürün Gözden Geçirilmesi


Anahtar Kelimeler: Endometrium kanseri, Kemik metastazı, Tedavi
INTRODUCTION

Endometrial carcinoma (EC) is one of the most common gynecological cancers of the female genital tract. About 90% of uterine cancers are adenocarcinoma.\(^1\) EC usually extends to cervix by local invasion and hematogenous dissemination is relatively infrequent. The usual sites for distant metastases are lung, liver, and brain.\(^3\) Isolated bone metastasis in EC is uncommon and is generally restricted to the pelvis and vertebrae. It is usually with abdominopelvic recurrences and/or other distant metastases. Isolated peripheral skeletal metastasis of endometrial cancer is very unusual.\(^2\) Herein, we present a case with stage IC endometrium adenocarcinoma that had isolated femur and tibia metastases following local radiotherapy and fractures despite of therapy.

CASE REPORT

A 62-year-old patient was admitted with postmenopausal bleeding to another hospital where she underwent surgical staging for EC, with total hysterectomy, bilateral salpingo-oophorectomy, infracolic omentum biopsy, bilateral para-aortic and pelvic lymph-node sampling and peritoneal washing, in September 2002. Findings were consistent with more than one half of the myometrial invasion, grade 1 and Stage IC disease, according to FIGO staging. Lymphovascular invasion was present. There was no family history for endometrial cancer. The patient underwent intracavitary irradiation for five days, but was readmitted to hospital 2 months after the surgery with left leg pain. There was no history of trauma. Physical examination was unremarkable. Plain radiographs of the distal femur and knee showed bone metastasis (Figure 1A). Bone scanning showed increased uptake at right distal femur, knee, ankle, and left proximal tibia (Figure 1B). An incisional biopsy was performed and pathology revealed metastatic adenocarcinoma (Figure 2A and B), which was positive for estrogen receptor and negative for progesterone receptor. Serum level of CA-125 was within normal range. Brain magnetic resonance imaging, a thoraco-abdominal computed tomography and mammography were unremarkable. Following local radiotherapy, medroxyprogesterone acetate and zoledronic acid was administered. After a month, spontaneous right proximal femur fracture occurred and surgical fixation was performed. New metastasis was detected on lumbar vertebra in February 2004 (Figure 1C) and palliative radiotherapy was given. Paclitaxel and carboplatin combination was given for 6 cycles at a dose of 175

![Figure 1. (A) Initial plain radiograph shows osteolytic lesions at the proximal and distal tibia (arrows). (B) Tc-99 bone scan shows increased uptake at right distal femur, knee, ankle and left proximal tibia (arrows). (C) Lateral view radiograph showing L3 vertebra metastatic lesion (arrow)](image)
mg/m² and AUC 5, respectively. During the follow-up period new bone lesions were detected and the patient was treated with radiotherapy.

**DISCUSSION**

EC is one of the most common gynecological cancers and it alone is expected to account for 6% of all new cancer cases among women.⁸ In 75% of cases, tumors are confined to the uterine body. EC most commonly spreads by direct extension to the adjacent tissues or lymphatic dissemination.¹ Hematogenous metastasis is less frequent in EC with lung being the most common site of metastatic involvement.⁹ Liver, bone, and brain metastases are less common.

The incidence of bone metastasis from recurrent EC is 4%.⁹ Abdul-Karim et al.¹⁰ reported the highest incidence, 25%, in a study of bone metastases from the sixty-seven autopsy cases with EC. Only six (8.7%) of these patients had known bone metastases while they were alive and all had high-grade carcinomas. The average survival from time of bone metastases to death was 6.6 months in these six patients. The range varied from 1 day to 15 months.¹⁰ Several case reports reported unusual bony sites for metastases from EC, such as the calcaneal, talus, metatars, humerus, mandible, skull (Table 1).²⁻⁷,¹¹⁻¹⁶ In evaluation of stage I cases, the range of time to bone metastasis varied from 4 months to 3 years.²,⁴,¹²,¹³,¹⁶ The survival was longer in cases with isolated bone metastasis, compared those with distant metastasis. However, Cooper et al.³ reported a case with metastatic endometrial carcinoma who survived more than five years with bone metastases on multimodality treatment: systemic chemotherapy and hormonal therapy for primary disease and local radiotherapy for metastasis, and stated that the presence of bone metastases found on the distal extremities is often associated with poor prognosis. Contrary to this hypothesis, Litton et al.² reported a case of isolated metastatic carcinoma to the calcaneal and talus from stage IA moderately differentiated adenocarcinoma treated with RT and ultimately below-knee amputation due to persistent ankle pain and a nonfunctional joint. After surgery, the patient was alive at the time of publication. The patient reported here developed bone metastases two months after the diagnosis of grade 1, stage IC EC and palliative irradiation to the left tibia and right femur with hormonal therapy were initiated. After nine months, paclitaxel plus carbop-

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**Figure 2.** (A) Well-differentiated endometrioid endometrial adenocarcinoma. (B) Histopathologic examination revealed adenocarcinoma within lamellar bone.
<table>
<thead>
<tr>
<th>Author name</th>
<th>Age</th>
<th>Primary tumor</th>
<th>Stage (FIGO)/grade</th>
<th>Time to progression after surgery</th>
<th>Metastatic site(s)</th>
<th>Treatment to bone metastases</th>
<th>Survival after bone metastasis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Litton et al., 1991</td>
<td>55</td>
<td>Moderately differentiated adenocarcinoma</td>
<td>IA/-</td>
<td>2 years</td>
<td>Right calcaneous, talus</td>
<td>Surgery, RT, below-the-knee amputation</td>
<td>&gt; 10 months</td>
</tr>
<tr>
<td>Maxymiw et al., 1991</td>
<td>63</td>
<td>Poorly differentiated adenocarcinoma</td>
<td>IV/-</td>
<td>4 months</td>
<td>Right mandible, lumbar spine, left hip, hilar, retroperitoneal, abdominal, supraclavicular lymph nodes</td>
<td>RT</td>
<td>3 months</td>
</tr>
<tr>
<td>Cooper et al., 1994</td>
<td>59</td>
<td>Moderately differentiated adenocarcinoma, adenosquamous carcinoma</td>
<td>IVB/2</td>
<td>Metastatic at the diagnosis</td>
<td>Right calcaneous</td>
<td>RT, DOX+CIS, MPA</td>
<td>&gt; 5 years</td>
</tr>
<tr>
<td>Schols et al., 1995</td>
<td>66</td>
<td>Poorly differentiated endometrial adenocarcinoma</td>
<td>IA/3</td>
<td>1.5 years</td>
<td>Humerus</td>
<td>Local RT, MPA</td>
<td>–</td>
</tr>
<tr>
<td>Petru et al., 1995</td>
<td>61</td>
<td>Well-differentiated adenocarcinoma</td>
<td>IVB/-</td>
<td>Metastatic at the diagnosis</td>
<td>Left tarsus</td>
<td>Lower leg amputation, CRB+CYC, MPA</td>
<td>&gt; 14 months</td>
</tr>
<tr>
<td>Malicky et al., 1997</td>
<td>44</td>
<td>Moderately differentiated adenocarcinoma</td>
<td>IVB/-</td>
<td>Metastatic at the diagnosis</td>
<td>Left proximal femur</td>
<td>Local RT, DOX+CIS, MPA</td>
<td>&gt; 2 years</td>
</tr>
<tr>
<td>Dosoretz et al., 1999</td>
<td>71</td>
<td>Moderately differentiated adenocarcinoma</td>
<td>IV/3</td>
<td>Metastatic at the diagnosis</td>
<td>Mandible</td>
<td>RT, TAX+ORB</td>
<td>&gt; 14 months</td>
</tr>
<tr>
<td>Sahinler et al., 2001</td>
<td>67</td>
<td>Undifferentiated adenocarcinoma</td>
<td>IC/-</td>
<td>2 months</td>
<td>Vaginal wall-left metatarsal bone</td>
<td>RT</td>
<td>2 months</td>
</tr>
<tr>
<td>Mustata et al., 2001</td>
<td>45</td>
<td>Moderately differentiated adenocarcinoma</td>
<td>IAV 2</td>
<td>3 years</td>
<td>Vagina, Lung, scalp, skull bone</td>
<td>Surgery to cranium, MPA</td>
<td>6 months</td>
</tr>
<tr>
<td>Manolitsas et al., 2002</td>
<td>76</td>
<td>Adenocarcinoma</td>
<td>IVB/3</td>
<td>Metastatic at the diagnosis</td>
<td>Lung, right calcaneous</td>
<td>Local radiotherapy, SERM, Liposomal DOX, external beam RT</td>
<td>11 months</td>
</tr>
<tr>
<td>Dursun et al., 2003</td>
<td>51</td>
<td>Endometrioid adenocarcinoma</td>
<td>IIIQ/3</td>
<td>1 month</td>
<td>Both humerus, left axillary lymph node</td>
<td>RT</td>
<td>&gt; 6 months</td>
</tr>
<tr>
<td>Ali et al., 2003</td>
<td>72</td>
<td>Poorly differentiated adenocarcinoma</td>
<td>IC/3</td>
<td>2 years</td>
<td>Lung, left fourth toe</td>
<td>RT, surgery, MPA</td>
<td>&gt; 16 months</td>
</tr>
<tr>
<td>Current Report</td>
<td>62</td>
<td>Well-differentiated adenocarcinoma</td>
<td>IC/I</td>
<td>2 months</td>
<td>Femur, tibia</td>
<td>RT, MPA, Zoledronic acid</td>
<td>&gt; 18 months</td>
</tr>
</tbody>
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RT: Radiotherapy, MPA: Medroxyprogesterone acetate, -: Unknown, DOX: Doxorubicin, CIS: Cisplatin, CRB: Carboplatin, CYC: Cyclophosphamide, TAX: Taxol, SERM: Selective Estrogen Receptor Modulatory
latin combination was administered with radiotherapy due to new metastasis on L3 vertebra. Thirty-three months after diagnosis of the initial bone metastases, new ones were detected.

Although EC is traditionally associated with local invasion and lymphatic dissemination, early onset of vertebral metastases have been reported to occur due to hematogenous spread via the Batson plexus. Early diagnosis and treatment of isolated bone metastasis of endometrium cancer is essential. Bone scans or conventional X-rays can be used for early detection of localized bone metastasis. Radiotherapy is the choice of treatment for bone metastasis, especially to those at risk for bone fracture. Palliative radiotherapy and platinum-based chemotherapy regimens followed by progestogens should be considered in patients with EC and bone metastasis for it has been shown to be effective in both preventing recurrence and prolonging survival.

REFERENCES


Correspondence
Dr. Mevlut KURT
Türkiye Yüksek İhtisas Eğitim ve Araştırma Hastanesi Gastroenteroloji Bölümü
Kızılay Sokak No: 2
06100, Şehittepe
Ankara / TÜRKİYE
Tel: +90.505 2762812
Fax: (+90.312) 312 41 20
E-mail: dr.mevlutkurt@gmail.com