

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 Türkiye Yüksek İhtisas 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

Endometrium kanserinin izole kemik metastazı çok nadirdir. Burada FIGO evre IC, grad I endometrium kanseri tanısı konulan, lokal radyoterapisi tamamlandıktan hemen sonra izole femur ve tibia metastazları saptanan 62 yaşında bayan hasta rapor edilmektedir. İnsizyonel biyopsi metastatik adenokarsinomu gösterdi. Radyoterapi sonrasında medroksiprogesteron asetat ve zoledronik asit verildi. Bir ay sonra, spontan sağ proksimal femur kırığı meydana geldi ve yeni kemik metastazı saptandı. Lokal radyoterapi ile 6 kür paklitaksel ve karboplatin kemoterapisi verildi, ancak kemik metastazları progresyon gösterdi. Bu makalede endometrium kanserli hastalarda gelişen kemik metastazları literatür eşliğinde tartışılmıştır.

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.¹ 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.²⁻⁷ 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

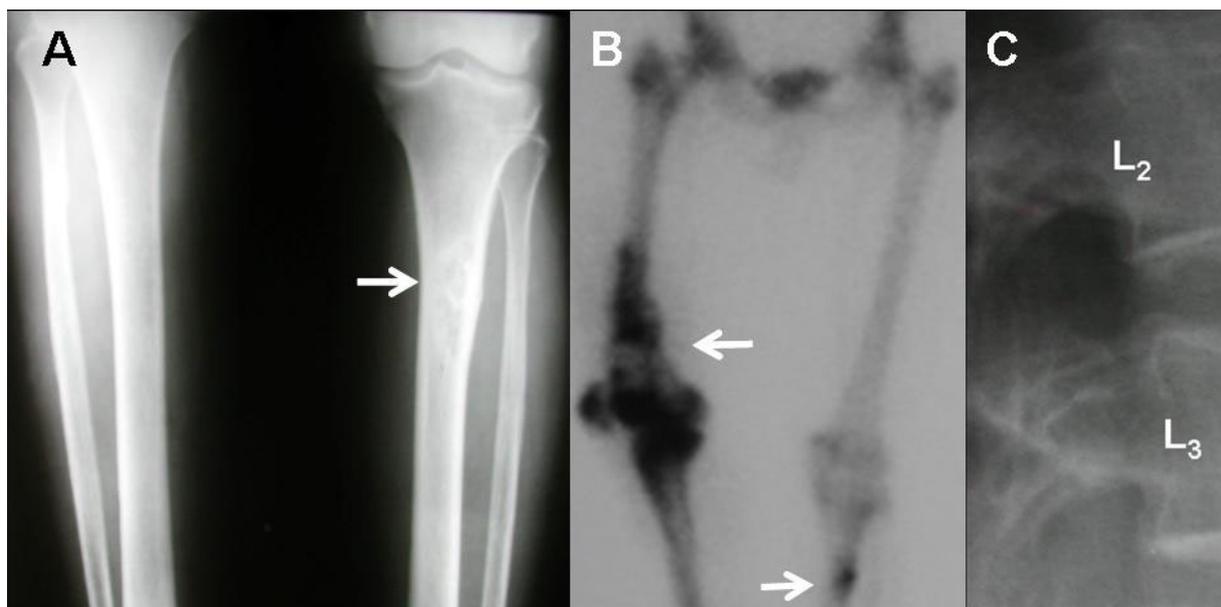


Figure 1. (A) Initial plain radiograph shows osteolytic lesions at the proximal and distal tibia (arrows). (B) Tc-99 bone scan shows increased uptake at right distal femur, knee, ankle and left proximal tibia (arrows). (C) Lateral view radiograph showing L3 vertebra metastatic lesion (arrow)

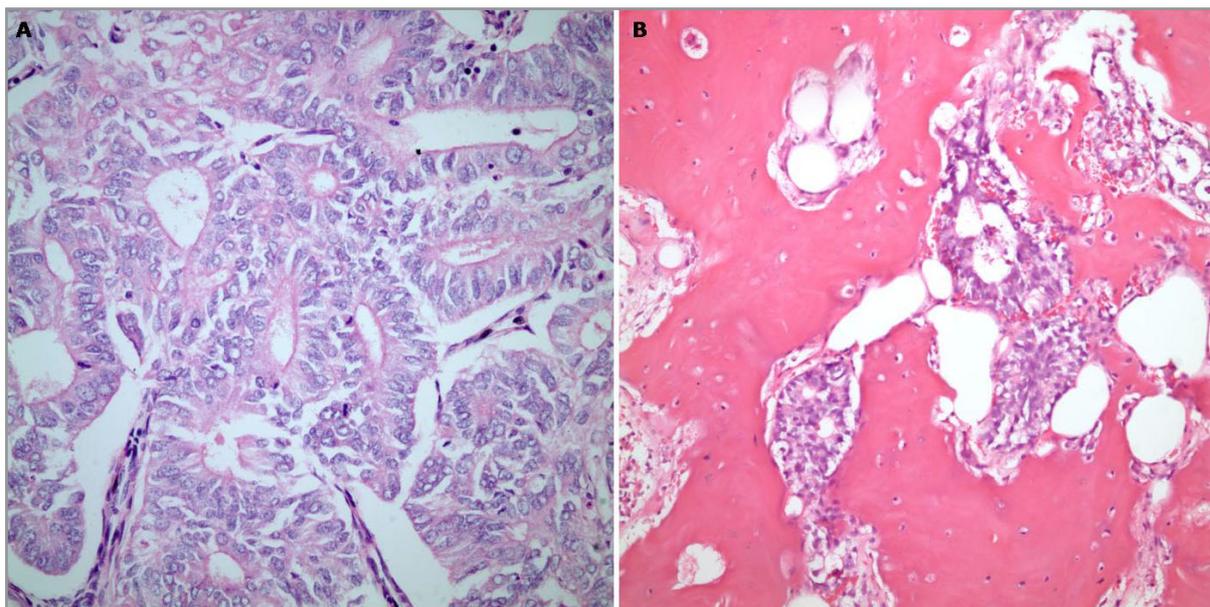


Figure 2. (A) Well-differentiated endometrioid endometrial adenocarcinoma. **(B)** Histopathologic examination revealed adenocarcinoma within lamellar bone.

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 calcaneus, 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 calcaneus 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-

Table 1. Endometrial adenocarcinoma and bone metastasis: Review of the literature

Author name	Age	Primary tumor	Stage (FIGO)/ grade	Time to progression after surgery	Metastatic site	Treatment to bone metastases	Survival after bone metastasis
1 Litton et al. ² , 1991	55	Moderately differentiated adenocarcinoma	IA/-	2 years	Right calcaneous, talus	Surgery, RT, below-the-knee amputation	> 10 months
2 Maxymiw et al. ¹¹ , 1991	63	Poorly differentiated adenocarcinoma	IV/-	4 months	Right mandible, lumbar spine, left hip, hilar, retroperitoneal, abdominal, supraclavicular lymph nodes	RT	3 months
3 Cooper et al. ³ , 1994	59	Moderately differentiated adenocarcinoma, adenosquamous carcinoma	IVB/2	Metastatic at the diagnosis	Right calcaneous	RT, DOX+CIS, MPA	> 5 years
4 Schols et al. ⁴ , 1995	66	Poorly differentiated endometrial adenocarcinoma	IA/3	1,5 years	Humerus	Local RT, MPA	-
5 Petru et al. ⁵ , 1995	61	Well-differentiated adenocarcinoma	IVB/-	Metastatic at the diagnosis	Left tarsus	Lower leg amputation, CRB+CYC, MPA	> 14 months
6 Malicky et al. ⁶ , 1997	44	Moderately differentiated adenocarcinoma	IVB/-	Metastatic at the diagnosis	Left proximal femur	Local RT, DOX+CIS, MPA	> 2 years
7 Dosoretz et al. ⁷ , 1999	71	Moderately differentiated adenocarcinoma	IV/3	Metastatic at the diagnosis	Mandible	RT, TAX+CRB	>14 months
8 Sahinler et al. ¹² , 2001	67	Undifferentiated adenocarcinoma	IC/-	2 months	Vaginal wall-left metatarsal bone	RT	2 months
9 Mustafa et al. ¹³ , 2001	45	Moderately differentiated adenocarcinoma	IA/ 2	3 years	Vagina, Lung, scalp, skull bone	Surgery to cranium, MPA	6 months
10 Manolitsas et al. ¹⁴ , 2002	76	Adenocarcinoma	IVB/3	Metastatic at the diagnosis	Lung, right calcaneous	Local radiotherapy, SERM, Liposomal DOX, external beam RT	11 months
11 Dursun et al. ¹⁵ , 2003	51	Endometrioid adenocarcinoma	IIIC/3	1 month	Both humerus, left axillary lymph node	RT	>6 months
12 Ali et al. ¹⁶ , 2003	77	Poorly differentiated adenocarcinoma	IC/3	2 years	Lung, left forth toe	RT, surgery, MPA	> 16 months
13 Current Report	62	Well-differentiated adenocarcinoma	IC/I	2 months	Femur, tibia	RT, MPA, Zoledronic acid	> 18 months

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

1. Burke TW, Mundt AJ, Muggia FM. Endometrial Carcinoma. In: Cancer: Principles and Practice of Oncology. DeVita VT, Hellman S, Rosenberg SA (eds). 7th ed. Philadelphia, Lippincott Williams & Wilkins, 2005: 1341-1360.
2. Litton GJ, Ward JH, Abbott TM, Williams HJ. Isolated calcaneal metastasis in a patient with endometrial adenocarcinoma. *Cancer* 67: 1979-1983, 1991.
3. Cooper JK, Wong FLW, Swenerton KD. Endometrial adenocarcinoma presenting as an isolated calcaneal metastasis. *Cancer* 73: 2779-2781, 1994.
4. Schols WA, Kock HC, van Etten FH. Recurrent endometrial adenocarcinoma presenting as a solitary humeral metastasis. *Gynecol Oncol* 59: 148-150, 1995.
5. Petru E, Malleier M, Lax S, et al. Solitary metastasis in the tarsus preceding the diagnosis of primary endometrial cancer. A case report. *Eur J Gynaecol Oncol* 16: 387-391, 1995.
6. Malicky ES, Kostic KJ, Jacob JH, Allen WC. Endometrial carcinoma presenting with an isolated osseous metastasis: a case report and review of the literature. *Eur J Gynaecol Oncol* 18: 492-494, 1997.
7. Dosoretz DE, Orr DE Jr, Salenius SA, Orr PF. Mandibular metastasis in a patient with endometrial cancer. Case report. *Gynecol Oncol* 72: 243-245, 1999.

8. Jemal A, Murray T, Ward E, et al. Cancer statistics, 2005. *CA Cancer J Clin* 55: 10-30, 2005.
9. Aalders JG, Abeler V, Kolstad P. Recurrent adenocarcinoma of the endometrium: a clinical and histopathological study of 379 patients. *Gynecol Oncol* 17: 85-103, 1984.
10. Abdul-Karim FW, Kida M, Wentz WB, et al. Bone metastasis from gynaecologic carcinomas: a clinicopathologic study. *Gynecol Oncol* 39: 108-114, 1990.
11. Maxymiw WG, Wood RE. Metastatic endometrial carcinoma to the mandible: a case report. *J Oral Maxillofac Surg* 49: 78-80, 1991.
12. Sahinler I, Erkal H, Akyazici E, et al. Endometrial carcinoma and an unusual presentation of bone metastasis: a case report. *Gynecol Oncol* 82: 216-218, 2001.
13. Mustafa MS, Al-Nuaim L, Inayat-Ur-Rahman N. Scalp and cranial bone metastasis of endometrial carcinoma: a case report and literature review. *Gynecol Oncol* 81: 105-109, 2001.
14. Manolitsas TP, Fowler JM, Gahbauer RA, Gupta N. Pain in the foot: calcaneal metastasis as the presenting feature of endometrial cancer. *Obstet Gynecol* 100: 1067-1069, 2002.
15. Dursun P, Gultekin M, Basaran M, et al. Bilateral bone metastasis in endometrial adenocarcinoma. *Lancet Oncol* 4: 547, 2003.
16. Ali ZA, Wimbhurst JA, Ali AA, et al. Endometrial cancer metastasis presenting as a grossly swollen toe. *Int J Gynecol Cancer* 13: 909-911, 2003.

Correspondence

Dr. Mevlut KURT
Türkiye Yüksek İhtisas Eğitim ve Araştırma Hastanesi
Gastroenteroloji Bölümü
Kızılay Sokak No: 2
06100, Sıhhiye
Ankara / TURKEY

Tel: +90.505 2762812
Fax: (+90.312) 312 41 20
E-mail: dr.mevlutkurt@gmail.com