American Journal of Case Reports

ISSN 1941-5923
© Am J Case Rep, 2015; 16: 473-477
DOI: 10.12659/AJCR.893978

Received: 2014.03.01
Accepted: 2015.04.06
Published: 2015.07.20

An Unusual Solitary Metatarsal Metastasis from an Endometrioid Endometrial Adenocarcinoma

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Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

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Conflict of interest: None declared

Patient: Female, 62
Final Diagnosis: Metatarsal metastasis from an endometroid endometrial adenocarcinoma
Symptoms: Painful • swelling hard mass • fixed to the underlying bone of the left foot
Medication: —
Clinical Procedure: Clinical and Gynecological examination • CT scan • left foot MRI • percutaneous core biopsy
Specialty: Oncology

Objective: Unusual clinical course

Background: Endometrial cancer is the fourth most common tumor in women. Abnormal uterine bleeding is the leading symptom in 90% of cases. The more frequent metastatic sites include lymph nodes, omentum, lungs, and liver. Bone metastasis has been reported to occur in 2–6% of all metastatic endometrial cancers, particularly in high surgical stage and grade, the most common involved site being the spine and hip.

Case Report: We report here the case of a 62-year-old white woman hospitalized for a painful swelling in the left foot, which appeared from January 2014, postmenopausal bleeding, and a progressive weight loss in the last year. An endometrioid, endometrial cancer was diagnosed by hysteroscopy, associated with a solitary bone metastasis of the left metatarsus, histologically confirmed by biopsy.

The patient refused any surgical procedure. She received a single-fraction of 800 cGy radiotherapy to the left foot, leading to optimal analgesic control. Subsequently, systemic chemotherapy was started using a carboplatin/paclitaxel-containing regimen with IV zoledronic acid. This treatment is ongoing.

Conclusions: There is no standard treatment for endometrial cancer bone metastasis. The prognosis of these patients is poor, with a median survival of about 12–17 months. The treatment is predominantly palliative and relies on several factors, including patient clinical conditions, site and number of bone metastases, and the presence of any additional visceral lesions. An aggressive multimodal treatment should be proposed to very select patients presenting better prognostic factors.

In our case, a solitary fifth metatarsal bone metastasis, histologically proved, was shown as initial presentation of an EC. Endometrial cancer can present as initial bone diffusion, even in atypical locations such as acrometastasis and it should be considered when bone metastases are diagnosed.

MeSH Keywords: Endometrial Neoplasms • Metatarsal Bones • Neoplasm Metastasis

Abbreviations: **EC** – endometrial cancer; **OS** – overall survival

Full-text PDF: http://www.amjcaserep.com/abstract/index/idArt/893978

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Background

Endometrial cancer (EC) is the most common gynecologic malignancy [1]. It usually affects post-menopausal women and in 90% of cases abnormal uterine bleeding is the initial symptom [1]. The 5-years overall survival (OS) is 80–90% [1]. The spread is typically from direct invasion or via the lymphovascular pathway [2].The incidence of stage IV disease is approximately 5–10% with a 5-year OS of less than 10%.

Bone metastases from EC are very uncommon and they have been reported to occur in 2–6% of all metastatic cancers [2]. Although an incidence of 25% has been reported in retrospective pathology series [3], only a few clinical cases of isolated bone metastases have been published [4–22].

The purpose of this case report is to describe an unusual and rare EC first presentation in a patient without any relevant risk factors for gynecologic cancers, showing an isolated metatarsal metastasis.

Case Report

In September 2014, a 62-year-old, white, non-smoker woman was hospitalized because of a painful, swollen, hard mass on the left foot, fixed to the underlying bone, which appeared in January 2014, along with postmenopausal vaginal bleeding and a weight loss of about 12 Kg in the last year.

The patient's history was uneventful and she had no relevant comorbidities. She had no pregnancies. Her past menstrual patterns had been regular and she never took any contraceptive pills. She underwent natural menopause at age 52 years. His body mass index (BMI) was 26 Kg/m^2.

Clinical examination showed a large, hard, and inflammatory lesion of the left foot (Figure 1A). Gynecological examination result was normal. X-ray imaging revealed a voluminous solid lesion of the fifth metatarsus, totally destroying the bone (Figure 1B). Abdominal-pelvic ultrasound documented an increase of endometrial thickness. At hysteroscopy, no suspected tumor lesion was shown. However, endometrial biopsy documented a grade II EC (endometrioid sub-type). The whole-body CT scan documented 2 lung nodules of 5.5 and 15 mm at greatest diameter. A bone scan revealed an increased radiotracer uptake within the fifth metatarsus without any other bone lesions. The Rx-mammography was normal. The left foot MRI confirmed the presence of a large, solid, tumor lesion of the fifth metatarsus, totally destroying the bone, compatible with a metastasis (Figure 1C, red arrows). A percutaneous core biopsy of this lesion was also performed revealing an adenocarcinoma metastasis consistent with the primary EC (Figure 1D). At the immunohistochemical staining, tumor cells were positive for estrogen receptor (Figure 1E) and negative for progesterone receptor, consistent with the diagnosis of an EC metastasis. The patient refused a whole body PET-scan. Laboratory test results were in the normal range and CA 125 was moderately increased at 81 UI/mL (NV <35 UI/mL). The patient refused any surgical procedure. She received also a single fraction of 800 cGy radiotherapy on the left foot, leading to optimal analgesic control. A pelvic radiation for the permanent vaginal bleeding was also suggested to the patient but it was not performed because of patient major anxiety. A systemic chemotherapy by carboplatin/paclitaxel regimen, associated with an IV zoledronic acid infusion, was started and is ongoing. Clinical evaluation after 3 cycles of chemotherapy showed a significant reduction of the metatarsal metastasis (Figure 2).

Discussion

EC is the fourth most common cancer in women in developed countries [1]. Metastatic EC lesions are predominantly found in the lymph nodes, omentum, lungs, and liver [1]. Bone metastases from EC are very uncommon and occur in 2–6% of all metastatic ECs [2]. Bone metastases at the first presentation (synchronous bone metastases) are extremely rare and they usually occur with disease recurrence [2, 23, 24]. In a recent retrospective study, an overall incidence of less than 1% was reported, with synchronous bone metastases representing only 0.12% of all patients [25]. The axial skeleton is the most common bone metastatic site, and isolated bone extremity metastases are extremely rare [2–24]. Although hematogenous dissemination is the most frequent mechanism involved in bone metastasis, a few cases of direct tumor extension have been described [2–24]. In a retrospective review, 21 patients with bone EC metastasis were identified [23]. Six patients (29%) presented a synchronous bone metastasis and 15 patients (71%) had a bone recurrence; in the latter case, the median time to bone metastasis recurrence was 10 months (range, 3–148). The OS of patients with synchronous bone metastases was 17 months as compared to 32 months for those with a bone metastasis recurrence [23].

More recently, in a retrospective analysis of 1632 EC patients, 19 (1.2%) presented a primary bone dissemination [24]. Three patients (15.8%) had synchronous bone metastases and in the others, median time to recurrence was 19.5 months (range, 3–114). The most common sites were the spine and hip. Concomitant visceral metastases were detected in 9 (47.4%) patients, whereas multiple bone metastases were found in 6 (31.6%). Nine patients (47.4%) had single-bone metastasis, 4 (21.1%) had single-bone metastasis with a concurrent visceral spreading, 1 (5.3%) had multiple (>2) bone metastases, and 5 (26.3%) had multiple, bone, and visceral lesions together.

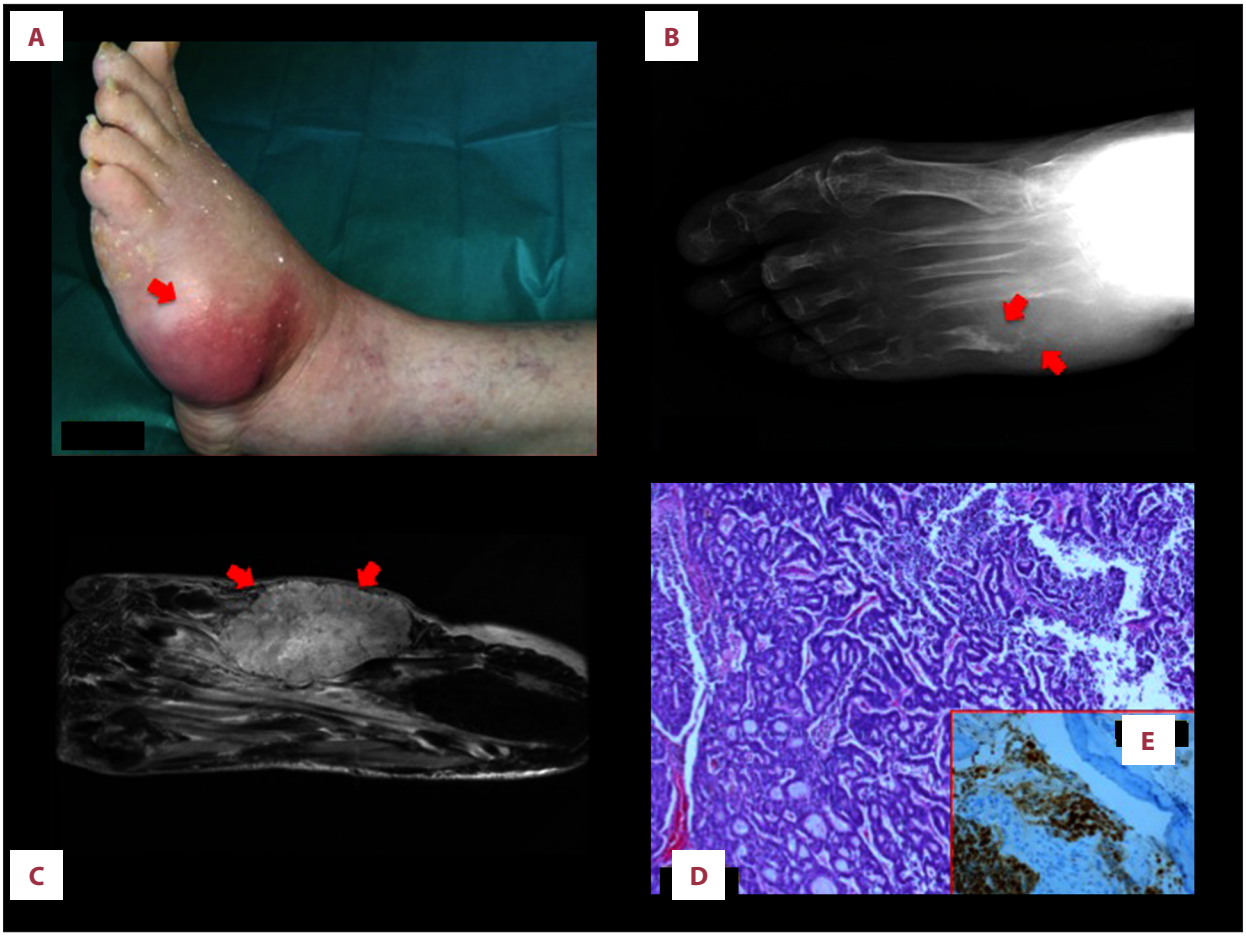

Figure 1. (**A**) Clinical examination shows a large inflammatory lesion on the left foot. (**B**) X-ray images document a large tumoral lesion of the fifth metatarsus totally destroying the bone (red arrows). (**C**) MRI reveals the presence of a large lytic tumor lesion centered on the fifth metatarsus, compatible with a bone metastasis (red arrows). (**D**) Histology shows tumor cells infiltrating the bone tissue, consistent with an EC metastasis. (**E**) On immunohistochemical staining, tumor cells are positive for the estrogen receptor, consistent with a diagnosis of EC metastasis.

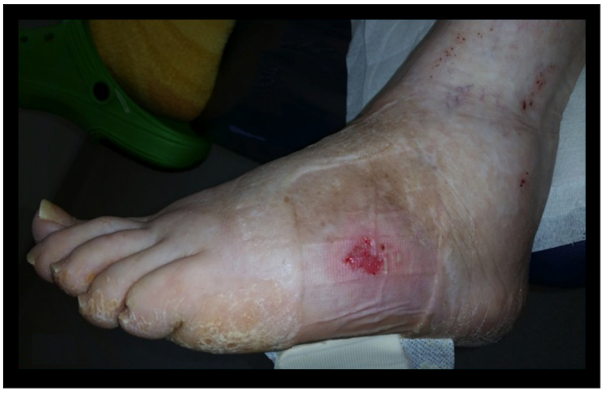

Figure 2. Clinical examination after 3 cycles of chemotherapy and local radiotherapy (a single fraction of 800 cGy), showing a significant reduction of the metatarsal metastasis.

Median OS was 12 months (range, 2–267). Multi-modal treatment improved median OS as compared to radiotherapy alone (20 *vs.* 33 months, respectively). Multiple bone involvement, extraosseous dissemination, and type II EC (serous or clear-cell histology) were associated with poor prognosis [24].

Usually, bone metastasis assessment is performed by bone scintigraphy. However, several other imaging methods are often used for diagnosing bone metastasis, including bone X-rays, CT scan, MRI, and PET-scan. In selected cases, cytological or histological confirmation is necessary [25].

There is no standard treatment for EC bone metastasis because of the small number of cases and the different patient characteristics described in the medical literature. However, the presence of concomitant visceral lesions seems to play a pivotal role in the decision-making strategy. The prognosis of these patients is poor, with a median survival of about 12–17

months [2–24]. The treatment is predominantly palliative and relies on several factors, including clinical patient condition, site and number of bone lesions, and the presence of concurrent visceral metastases. Based on the literature data, the most common treatment of bone metastases involves surgical resection of the accessible lesion, stereotaxic or palliative radiotherapy, radiofrequency with cementoplasty, and systemic chemotherapy or hormonotherapy [2–25]. In addition, bisphosphonates or denosumab can be added [2–25]. Solitary bone metastasis seems to be associated with a better prognosis and must guide a more aggressive treatment [2–25].

Conclusions

In our case, a solitary fifth metatarsal bone metastasis, histologically confirmed, was shown as the initial presentation of an EC. Our literature review revealed only a few cases of primary EC bone metastasis and all were symptomatic at diagnosis. Isolated bone metastasis is extremely rare and unusual. As in our case, there were usually concomitant gynecologic symptoms, such as abnormal vaginal bleeding, leading to EC diagnosis. However, in contrast with the majority of other reported cases where primary endometrial tumor was locally advanced and easily diagnosed by conventional imaging techniques, in this case only an increase of endometrial thickness was documented at the abdominal-pelvic ultrasound. Hysteroscopy found no suspected tumor lesion but endometrial biopsy confirmed a grade II EC (endometrioid sub-type).

Because the patient refused all surgical procedures and due to the presence of 2 small suspected concomitant lung lesions, she underwent site-directed palliative radiation therapy, systemic chemotherapy with a carboplatin/paclitaxel-containing regimen, and zoledronic acid administration. The local radiotherapy highly improved her foot pain.

EC can present as initial bone diffusion, even in atypical locations such as acrometastasis and it should be considered when bone metastases are diagnosed. Appropriate imaging techniques, such as bone scintigraphy, CT, MRI, bone, and PET scan should be used to confirm this diagnosis. However, a bone biopsy should be done to clarify the clinical situation.

There is no standard treatment, and treatment selection should consider several factors, including clinical patient conditions and comorbidities, site and number of bone lesions, presence of additional visceral metastases, EC sub-type, and the time to recurrence. A multimodal and more aggressive treatment should be proposed for very selected patients presenting with better prognostic factors.

Competing interests

There are no competing interests to declare.

Acknowledgments

We would like to thank Mrs. Nadia Ouamara for the English revision and Dr. Nicolas Hamant and Mr. Yves Soulatges for the acquisition of histology images.

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