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Unusual Presentation of Endometrial Cancer: A Clinicopathological Study of One Case

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Abstract

Endometrial carcinoma is the most frequent genital tract malignancy. The first symptom (guide-symptom) is usually metrorrhagia; however, in around 10% of cases it is not. In contrast, osseous metastases are infrequent in endometrial cancer. The bones of the pelvis and lower extremities are those most frequently involved in disseminated metastatic diseases. In these cases, endometrial cancer is usually high grade (Grade III). Case report: 56-year-old woman who presented right inguinal pain. The X-ray showed a lithic lesion in the right ischium. A histopathological study demonstrated a metastatic lesion, suspected to be endometrial cancer. The computer tomography scan revealed a uterine mass and a second lithic lesion in the right tibia. The patient received chemotherapy (carboplatin and paclitaxel), and the bone lesions were irradiated. The patient is still alive 18 months after the diagnosis. This case emphasizes the importance of considering an endometrial primary tumor when evaluating bone metastasis of unknown primary cancer.

Keywords

Osseous Metastasis, Endometrial Carcinoma, Immunohistochemistry

1. Introduction

Endometrial cancer is the most common genital tract malignancy [1] in women, and its frequency is approx-

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imately the same as that of all other female genital tract malignancies combined. Around 90% of the cases are sporadic while the remaining 10% are hereditary [2]. In 1983, Bokham proposed a dual model (type 1 and type 2) for the classification of these tumors on the basis of a distinct carcinogenetic pathway. Type 1 is the most common variant. Occurring in pre- and post-menopausal women, type 1 is a hormone-dependent neoplasia related to pre-neoplastic lesions such as endometrial hyperplasia. Type 2 or serous carcinoma is a less frequent tumor. It occurs in older women, and no morphological pre-neoplastic lesions have been defined. Type 2 is a high-grade tumor, and the prognosis is poor [3].

Metrorrhagia is the most common first symptom related to endometrial carcinoma in pre- and post-menopausal women. However, around 10% of cases do not present uterine bleeding. These cases may simulate other primary tumors. Consequently, the consideration of metastasis from endometrial carcinoma should be included in the differential diagnosis of these cases. Bone metastases are more common in late stages of endometrial cancer, and they indicate proliferation and aggression [4]-[6]. Here we describe a case of endometrial carcinoma with an unusual presentation as primary osseous tumor.

2. Case

A 56-year-old woman complained of disabling right inguinal pain. A traumatic episode had occurred 8 months earlier. The X-ray examination of her pelvis revealed a 7-cm osteolytic lesion with cortical insufflation on the right ischium (**Figure 1**). Aspirative biopsy of the lesion was performed. After the histopathological diagnosis, a bone scan showed another increased uptake in the right femur (**Figure 2**), and the computer tomography (CT) scan revealed a uterine mass. No other tumoral lesions were demonstrated. Endometrial curettage was performed. The patient received chemotherapy (carboplatin and paclitaxel) for 6 months, and the bone lesions were irradiated. Nine months after the treatment had finished, a sacrococcygeal tumoral mass appeared and was accompanied by pain. The patient was treated with doxorubicin for three months. The CT-SCAN demonstrated tumoral necrosis but the pain persisted. In the last control performed (28 months after the first diagnosis), ten months after the second treatment had been completed, an inguinal lymph node appeared and was interpreted as progression of the disease. The patient was not attended to hospital at this point.

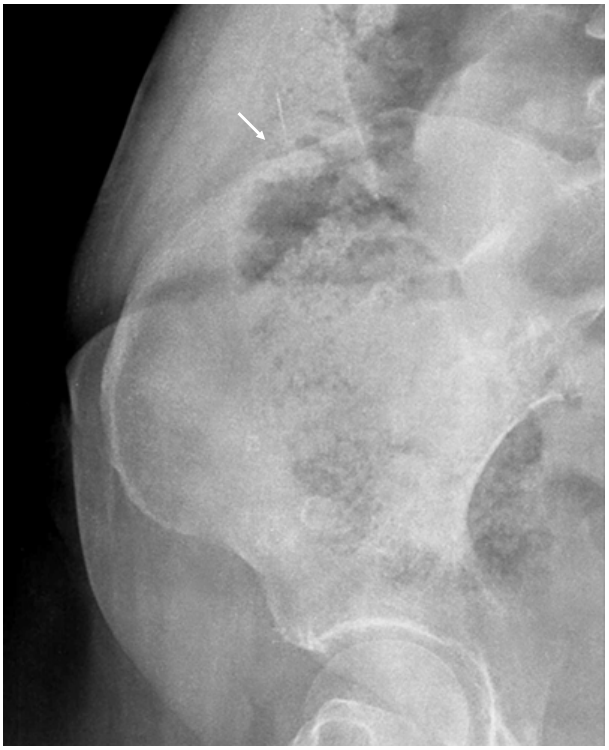

Figure 1. The pelvic X-ray shows an osteolytic lesion with cortical insufflation located in the ischium.

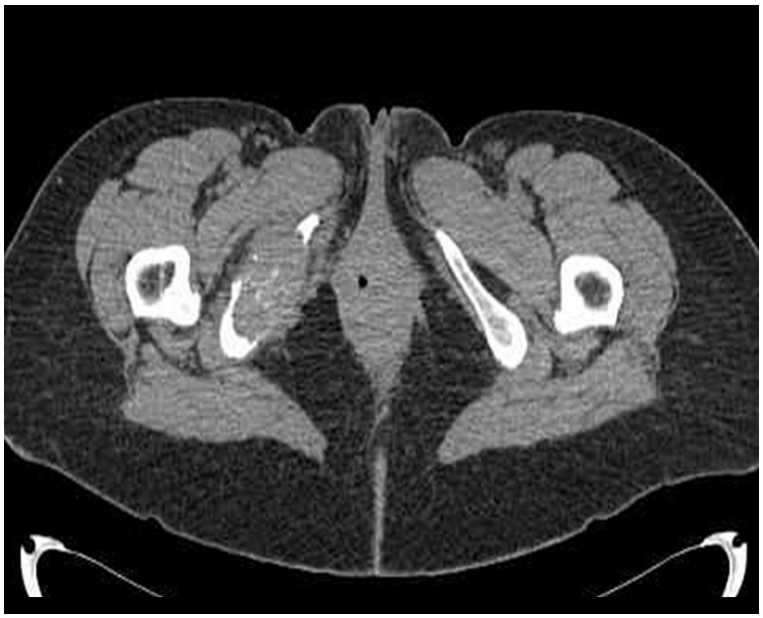

Figure 2. The computed tomography scan of the pelvis confirms the presence of an ischium-pubic lesion that breaks through the cortical bone and affects the surrounding soft tissue.

Tissue from the sample was fixed in 4% buffered formalin for a minimum of 24 h for normal histology and immunohistochemistry. We then took 3-µm sections from paraffin-embedded blocks and stained them with HE. A biopsy confirmed the suspicion of metastasis. The histological study demonstrated an epithelial proliferation with some glandular structures (**Figure 3**). The differential diagnosis pointed to a gynecological, pancreatic, or intestinal tumor. An immunohistochemical study was performed using the antibodies listed in **Table 1**, demonstrating the expression of high molecular weight cytokeratin and low molecular weight cytokeratin (AE1-AE3, 34βE12, Cam5.2 and cytokeratin 7), estrogen receptors, and progesterone receptors. No expression of CDX2, cytokeratin 20 (Excluding large bowel primary tumor), TTF-1 (Excluding lung primary tumor), vimentin, or CD10 (excluding primary kidney tumor) was detected (**Figure 4**). The diagnosis was a metastasis of well differentiated (Type I), endometrioid adenocarcinoma. The histopathological study of the endometrial curettage confirmed the origin of the tumor (**Figure 5**).

3. Discussion

Endometrial cancer is the most common genital tract malignancy [1], type 1 being the most prevalent. The vast majority of type1 cases have low grade (Grade 1) tumors, and the disease is diagnosed in early stages, thus generating the perception that it is relatively non-aggressive. However, some cases initially present metastatic disease, without the classical symptoms of this type of cancer (metrorrhagia) [4]. In these cases, like the present one, there is an added difficulty for the pathologist because of the unusual presentation of the disease. On the basis of only the first signs of the disease, we could have overlooked the endometrial carcinoma as a first option in the differential diagnosis.

The case was uncommon, as bone metastasis is found with solid tumors but seldom with endometrial cancer (2% - 6%), [5] [6] and even more rarely as a presenting symptom. The incidence of osseous metastasis from endometrial cancer is very low [5] [6]. Furthermore, bone metastases can mimic other benign conditions. It is therefore important to consider this possibility in a patient with skeletal pain who is not responding to conservative measures. The interval from initial diagnosis of endometrial carcinoma to bone metastasis is on average three years [5], and the carcinoma is usually seen with abdominopelvic recurrences and/or other organ metastases, such as lung and liver [6]. The average survival rate with bone metastasis is between 32 and 36 months depending on the series [4]-[6]. Our patient was alive 28 months after the diagnosis.

Endometrial tumors usually spread to the vertebrae and pelvic bones via the Batson plexus and systemic

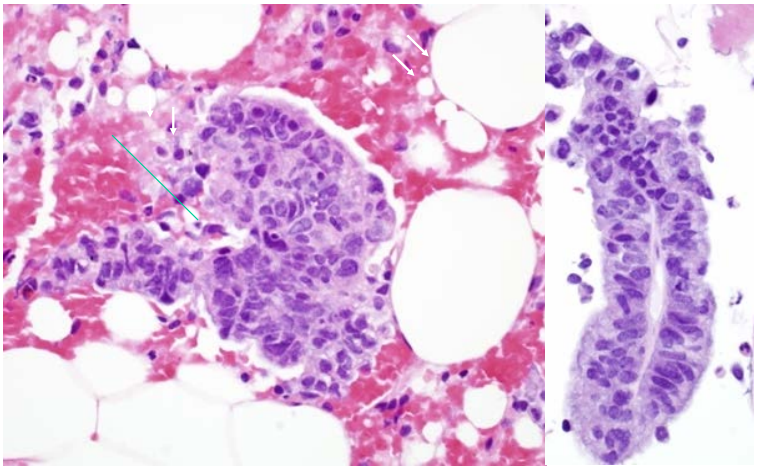

Figure 3. (H & E 40×) Histological analysis reveals groups of cohesive cells with elongated and hyperchromatic nuclei in the ischium bone marrow that occasionally form glands.

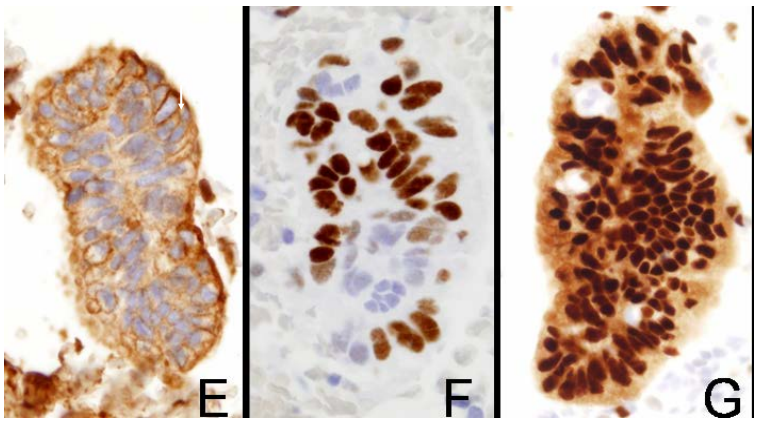

Figure 4. Tumor cells show expression of cytokeratin AE1-AE3 (E 40×), estrogen receptors (F 40×), and progesterone receptors (G 40×).

Table 1. Antibodies used in the immunohistochemical study and results.

ANTIBODY	CLONE	ANIMAL	SUPPLIER	RESULT
CK AE1-3	AE1-3	MOUSE	NOVOCASTRA	+
CKCAM 5.2	CAM 5.2	MOUSE	VENTANA	+
CK7	SP52	RABBIT	VENTANA	+
CK20	SP33	RABBIT	VENTANA	−
Ck HMW	34Be12	MOUSE	VENTANA	+
ER	SP1	RABBIT	VENTANA	+
PR	1E2	RABBIT	VENTANA	+
CD10	SP67	RABBIT	VENTANA	−
VIM	V9	MOUSE	VENTANA	−
CDX2	EPR2764Y	MOUSE	VENTANA	−
TTF1	SP141	RABBIT	VENTANA	−

VENTANA, Tucson Arizona, USA. DAKO Glostrup, Denmark. NOVOCASTRA, Newcastle, UK. Heat was used as the retrieval method for all antibodies.

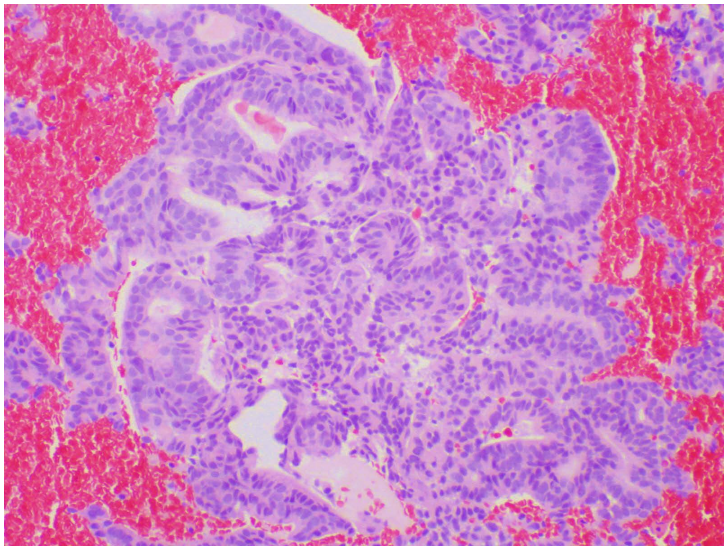

Figure 5. (H & E 40×) Well-differentiated (Grade 1) endometrioid endometrial-adenocarcinoma. Curettage.

vertebral venous plexus. The spread to the limbs occurs in a hematogenous manner [5]. Isolated bone lesions in the lower extremities are extremely rare [5], although the bones most frequently involved in metastatic endometrial carcinoma are those of the feet, mainly the calcaneus. Metastases to the metatarsus, tarsus, tibia, fibula, femur, ischium, vertebrae, humerus, mandible, and cranium have also been described [5] [6]. In late stages of the disease, bone metastases are more common and reflect dissemination and aggression [5] [6]. The majority of these tumors are high-grade endometrial carcinomas (Grade III or undifferentiated carcinomas] and in the variable stage at diagnosis [6]; however, they may be low-grade endometrial endometrioid carcinomas, like the present case. Osseous metastases can be associated with visceral metastasis, but rarely appear as a primary symptom. The present case is an example that symptoms related to metastatic bone lesion can occur as a primary symptom of endometrial carcinoma.

4. Conclusion

In conclusion, we believe that the pathologist should consider endometrial cancer in cases of bone metastatic lesions when uterine bleeding is not present. However, further research is required in order to detect the 10% cases that do not show the common signs of this disease.

Conflict of Interest

The authors declare no conflicts of interest regarding the paper submitted.

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