

Research Letter

## Limb salvage treatment in a 25-year-old woman with stage IVB endometrial cancer presenting with hip bone metastasis

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Accepted 2 May 2012

Endometrial cancer is typically diagnosed at an early stage and is seen mainly in postmenopausal women who present with abnormal uterine bleeding [1]. The presence of Stage IV endometrial cancer at the time of the initial diagnosis is uncommon, and such patients generally have a poor prognosis. The management of these patients remains a clinical dilemma, although it has been advocated that treatment should be individually tailored according to the main site of extrapelvic spread. A previous study that examined a large number of patients with stage IVB endometrial cancer who underwent primary surgical cytoreduction ( $n = 65$ ) revealed that the median survival of the optimally cytoreduced group was 34 months compared to 11 months for the suboptimally cytoreduced group [2]. Here, we report the case of a very young patient with Stage IVB endometrial cancer who was successfully treated after undergoing a comprehensive assessment.

In 2007, a 25-year-old nulliparous woman presented with an unstable gait that had been present for 3 weeks. She visited an orthopedic outpatient clinic because she was suffering from progressive left hip pain. The physical examination at this time revealed limited range of motion of the left hip joint. Magnetic resonance imaging (MRI) was performed because it was suspected that the patient was suffering from femoroacetabular impingement syndrome. This analysis showed enhanced soft tissue in the left ischium and at the junction of the left acetabulum located anterior to the column-superior pubic rami in addition to bony cortex destruction (Fig. 1).

Abdominal computed tomography (CT) revealed bilateral iliac lymphadenopathy and ascites, together with osteolytic bony lesions in the pelvic cavity. Positron emission tomography (PET) confirmed lymphadenopathy at the paraaortic and bilateral iliac lymph nodes and lesions in the left hip (Fig. 2). CT-guided biopsy of the left acetabulum revealed a poorly differentiated metastatic carcinoma (Fig. 3). An analysis of the family history of the patient revealed that the patient's mother and uncle (her mother's brother) had colon cancer and that her grandfather had gastric cancer. Due to the suspicion of hereditary nonpolyposis colorectal cancer (HNPCC, Lynch syndrome), a colonoscopy and a breast ultrasound were performed, both of which yielded negative findings. The patient received a gynecological oncology consultation, although she denied experiencing any menstrual abnormalities. Intriguingly, a hysteroscopy revealed the presence of multiple endometrial polypoid lesions that were diagnosed as a poorly differentiated adenosquamous carcinoma. She underwent cytoreductive surgery for advanced endometrial cancer that included a total hysterectomy, bilateral salpingo-oophorectomy, bilateral pelvic and para-aortic lymph node dissection, appendectomy, omentectomy, and multiple intraperitoneal excisional biopsies. The patient was optimally debulked with no gross residual tumor at the conclusion of the surgery. The histopathological analysis confirmed the presence of a Grade 3 endometrioid adenocarcinoma with squamous differentiation, 80% myometrial invasion, and metastases to the bilateral pelvic and para-aortic lymph nodes and the peritoneal surface of the urinary bladder and the cul-de-sac. Immunohistochemical analysis revealed that the tumor was negative for estrogen receptors, progesterone receptors, HER-2/*neu*, and epidermal growth factor receptors. The patient received adjuvant concurrent chemoradiation (CCRT)

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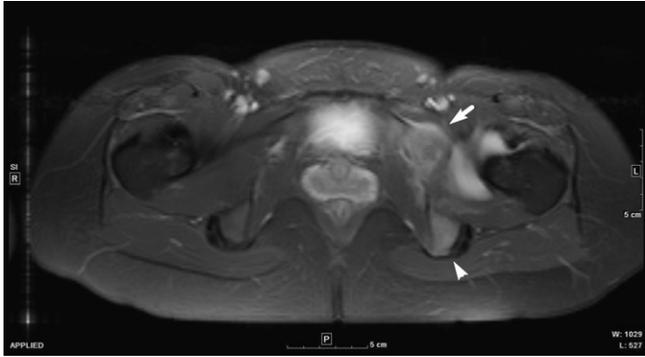


Fig. 1. An axial fat-suppressed contrast-enhanced T1-weighted MR image of the pelvis showed enhancing soft tissue at the left acetabulum (arrow) and the left ischium (arrowhead), along with bony cortex destruction.

with cisplatin 75 mg/m<sup>2</sup> and paclitaxel 175 mg/m<sup>2</sup> every 3 weeks for 6 cycles plus radiotherapy consisting of 5040 cGy in 28 fractions to the pelvic region and the metastatic bony lesions. The metastatic lesions were further targeted by image-guided radiotherapy consisting of 2000 cGy/10 fractions (total dose: 7040 cGy). The patient tolerated the regimen well, and serial imaging studies (including CT and PET scans, tumor markers, and bone biopsy) performed 42 months after CCRT showed no evidence of recurrence. Four years later, she has remained disease-free without joint dysfunction.

To our knowledge, our patient represents the youngest patient to date to have been diagnosed with stage IVB

endometrial cancer with bone metastases. Intensive cytoreductive surgery, adjuvant CCRT, and irradiation to the local bone metastases resulted in long-term disease-free survival. In the medical literature, the youngest such patient to be reported previously was a 32-year-old; her case was reported 5 months after diagnosis, at which time she was alive but continued to suffer from the disease [3].

Cases of endometrial cancer with bone metastases are rare, and such findings at the time of diagnosis are even more uncommon [3]. However, these patients are typically diagnosed in the postmenopausal period [3,4]; the reported ages of these patients range from 32 to 84 years. The sites of bone metastasis can vary and include the skull, vertebrae, sacrum, ischium, humerus, femur, fibula, tibia, calcaneus, and mandible [4]. The process by which these tumors metastasize to bone remains unclear, although hematogenous dissemination has been suggested as a potential mechanism [3,5]. The prognosis of patients with endometrial cancer and bone metastases is poor, and these patients typically succumb within 2 years of diagnosis [3]. However, 2 patients were reported to have survived for 5 years at the time the reports were made [6,7].

As the symptoms of endometrial cancer with bone metastases mimic those of other benign orthopedic diseases, a diagnosis is often difficult, and clinicians should consider this type of endometrial cancer as a potential diagnosis for patients presenting with bone pain. An analysis of the reported cases of bone metastasis in endometrial cancer reveals that many of these cases present with complicated clinical

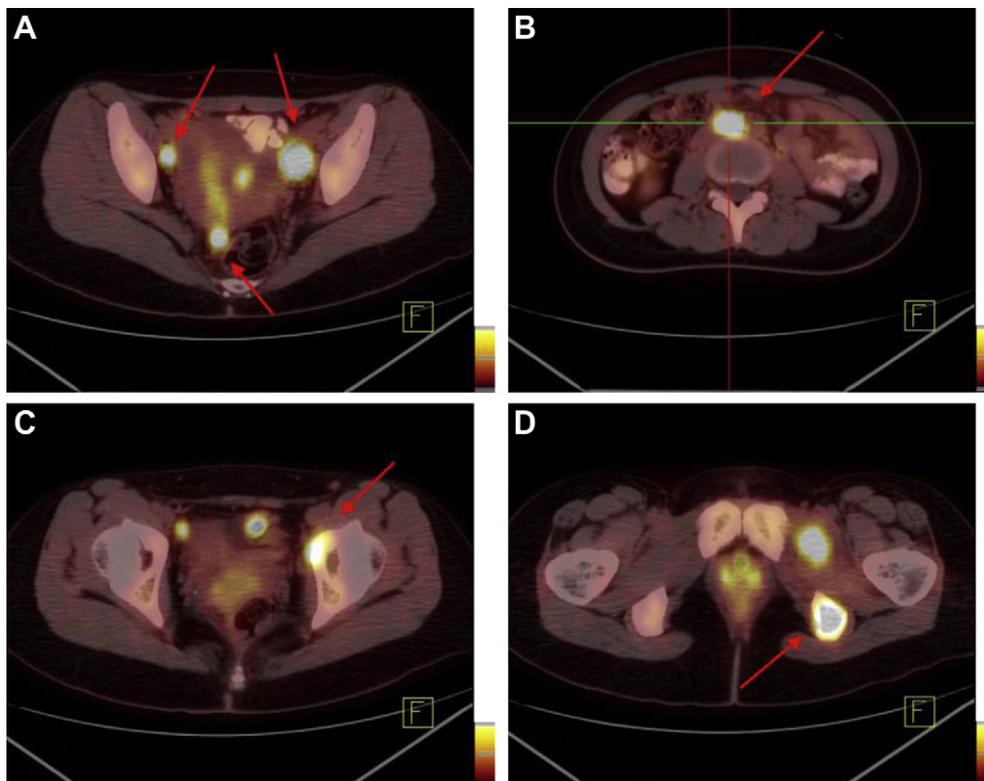


Fig. 2. Positron emission tomography-computed tomography showed increased uptake at (A) the bilateral iliac lymph nodes and the left presacral soft tissue, (B) the para-aortic lymph nodes, (C) the left acetabulum, and (D) the left ischium. The red arrows reveal the lesion sites.

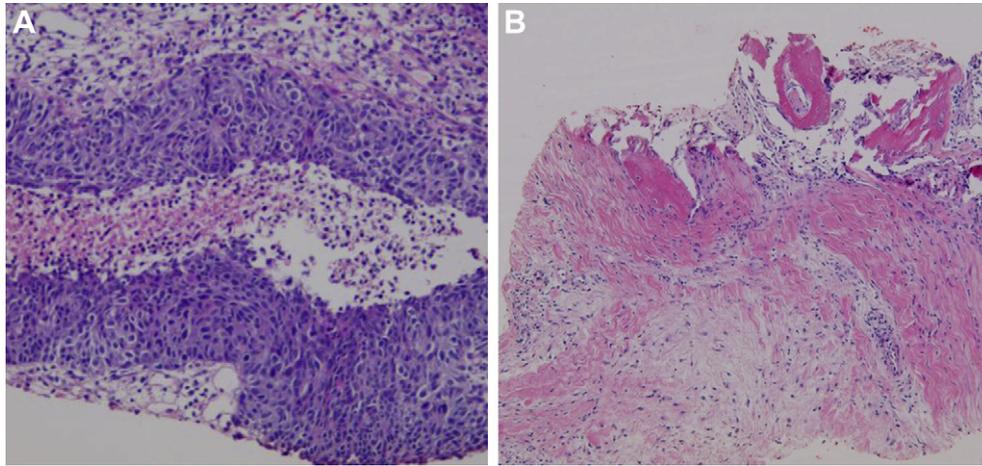


Fig. 3. (A) Biopsy of the left acetabulum lesion revealed poorly differentiated carcinoma with necrosis. (B) Normal bone histology for comparison. Hematoxylin and eosin stain, magnification 200 $\times$ .

manifestations (without abnormal uterine bleeding) that result in bone metastasis, which are only diagnosed after post-surgical staging [5]. Moreover, it is also quite common to encounter patients with bone pain of unknown origin whose endometrial cancer is only discovered following radiation treatment of the bone metastasis [8,9]. Therefore, it is essential to investigate the history of the patient carefully and to have a high index of suspicion. Appropriate imaging analyses, such as CT, MRI, and PET scans, should prove useful for clarifying these clinical dilemmas [3,10].

Radiation of the metastatic bony lesion is effective for both pain relief and disease control [4,9]. However, surgical resection should be reserved for special cases, such as for those where calcaneal or ischial amputation is possible [6,10]. The combination of systemic chemotherapy and local radiotherapy is suggested for patients with multiple bone metastases and intra-abdominal diseases [5]. However, treatment should be performed on a case-by-case basis.

The patient described here was strongly suspected as having an HNPCC-related cancer [11]. However, this study was limited by the lack of genetic testing; such testing was not performed because the effectiveness of screening for mismatch repair genes is currently unproven for cases of endometrial cancer [11]. However, clinicians should bear in mind that patients who belong to an HNPCC family might be more likely to develop early-onset cancers, including colorectal cancer and cancers of the endometrium, stomach, ovary, hepatobiliary tract, small bowel, upper urinary tract, and brain. The lifetime risk for developing endometrial cancer is estimated to be 40% to 60% [11]. At present, a multimodal endometrial screening strategy is emphasized, whereby endometrial sampling in individuals between the ages of 30 to 35 years in addition to an annual transvaginal ultrasound may improve the detection of endometrial cancer or hyperplasia in asymptomatic women who belong to an HNPCC family [11, 12]. Hysteroscopy has also been shown to be useful for detecting premalignant lesions in asymptomatic women [11].

Although this condition is rare, this report serves to emphasize that clinicians should be aware of the possibility of encountering female patients with early-onset endometrial cancer metastases who have no gynecological complaints. To obtain a successful outcome, comprehensive and individualized treatment should be pursued.

#### Acknowledgments

This study was supported by grants from the Department of Health (DOH99-TD-B-111-005 to CHL; DOH99-TD-C-111-006 to AC).

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