Sacral metastases in an endometrial cancer patient after treatment with sequential chemo-radiotherapy: a case report

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SUMMARY

The incidence of bone metastases in endometrial cancer is reported to occur in less than 15% of patients with metastatic disease. The medical literature is limited to only case reports, although none describing a sacral recurrence after adjuvant chemo-radiation therapy. We present the case of a 64-year-old woman who underwent surgery for endometrial adenocarcinoma followed by "sandwich" chemoradiation therapy at our institution, July 2006 (FIGO stage IB grade 3). In spite of adjuvant therapy, which was delivered in August 2008 the patient, developed an isolated sacral recurrence. The optimal therapeutic modality for endometrial cancer patients with high-risk disease remains controversial. The increasing use of combined modality therapy for early stage, high-risk patients may produce different recurrence patterns than described in historical controls.

KEY WORDS: *Endometrial Neoplasms; Neoplasm Recurrence, Local; Bone Neoplasms; Neoplasm Metastasis; Antineoplastic Agents; Radiotherapy; Combined Modality Therapy*

INTRODUCTION

Endometrial cancer with metastases to the bone is reported to occur in less than 15% of patients with metastatic disease (1). We present the case of a patient diagnosed with early stage, high-risk endometrial adenocarcinoma that developed a recurrence in the sacrum after surgery and adjuvant sequential chemotherapy and radiation therapy.

CASE REPORT

A 64-year-old woman underwent surgical staging for a T1bN0M0[1] (FIGO[2] Stage IB) endometrial adenocarcinoma, during July 2006. Histopathologic examination confirmed a poorly differentiated (FIGO grade 3) endometrioid adenocarcinoma. The tumor occupied the entire endometrial cavity (4 x 3 cm) and invaded 6 mm of the myometrium (total 20 mm). Vascular invasion was detected. The fallopian tubes, ovaries, and lymph nodes (10 nodes) were unaffected.

The patient received adjuvant treatment with sequential chemotherapy and radiation therapy. Six cycles of chemotherapy "sandwiched" with external beam whole pelvic radiation was administered. Chemotherapy was initiated 47 days from the time of surgery; it consisted of paclitaxel and carboplatin administered every 21 days at doses of 175 mg/m^2 and an AUC 5, respectively (3 cycles before and after radiation therapy). Radiotherapy was initiated 124 days after the completion of surgery and consisted of 50.4 Gy to the pelvis utilizing 15 mV photons in a 4-field technique given at 1.8 Gy per day fractions. Irradiation of the pelvis was completed in 5 weeks and resulted in minimal toxicities such as urinary urgency and diarrhea. Within four weeks of completing radiotherapy, the patient initiated her final 3 cycles of chemotherapy and was able to complete all chemotherapy without dose delays or reductions.

The patient was clinically and radiographically disease-free until August 2008. After a complaint of hip and pelvic pain, MRI examination (including gadolinium contrast) of the pelvis and lower extremities and whole body scintigraphy (approximately 30 mCi of Tc-99m MDP) were done. The images showed sacral metastasis consistent with recurrent disease. Histopathologic evaluation of the lesion confirmed compatibility with recurrence of the primary lesion.

DISCUSSION

This report describes a recurrence of endometrial adenocarcinoma in the sacrum of a patient diagnosed with early stage, high-risk endometrial cancer two years after the completion of sequential chemotherapy and radiation therapy.

Distant endometrial cancer metastases most commonly involve the lung, liver, bone, and brain (2). Although autopsy data show an incidence of bone metastases as high as 25%, the clinical incidence is reported to be only 2%-6% of patients with endometrial cancer (1,3). The diagnosis of bone metastases from endometrial cancer is most commonly seen approximately 3 years from the time of initial diagnosis (4). The appendicular skeleton appears to be most commonly involved; while the axial skeleton is limited to only a few cases in the literature (cervical vertebra (1), thoracic vertebra (1), and sacrum (1)) (1).

Our report describes the first case of a patient with sacral metastases occurring in an endometrial cancer patient following adjuvant sequential chemotherapy and radiation therapy. The only other report of sacral metastases is given by Albareda et al. (1). They reported on a patient with FIGO stage IB grade 1 endometrial adenocarcinoma that, after treatment with surgery alone, developed a solitary recurrence in the sacrum.

The optimal therapeutic modality for early stage, high-risk endometrial cancer is controversial. Administration of some form of radiation therapy has been the usual practice. Whole pelvic radiation therapy prescribed in the adjuvant setting is typically delivered at a dose of 50.40 Gy given no more than 28 fractions of 1.8 Gy per fraction (5). Trials involving radiation therapy typically require initiation of treatment within 56 days from the time of surgery (5). However, in our patient, the delivery of chemotherapy prior to radiation therapy may have resulted in a delay in locoregional treatment that may have produced in an increased risk for failure. In GOG 99, Keys et

1 International Union Against Cancer / American Joint Committee on Cancer
2 International Federation of Gynecology and Obstetrics

al. reported, during a median follow-up of 69 months, no bone failures in the radiation therapy arm (5). The delay in radiation therapy to the pelvis during chemotherapy administration may have allowed asymptomatic progression of disease that was poorly controlled with the sequential treatment regimen (6).

Chemotherapy appears to be emerging as a potentially important adjuvant treatment in endometrial cancer patients. In advanced disease, chemotherapy may offer a survival benefit over radiation, but radiation has consistently reduced the risk of pelvic recurrence (7-10). The most influential was GOG trial 122, a randomized control trial (RCT) comparing whole-abdominal irradiation (WART) to chemotherapy in stage III or IV endometrial carcinoma. Recurrence rates in the chemotherapy arm of GOG 122 were 50% overall. Although information regarding pelvic bone metastases was not given, 35% of the initial recurrences were limited to the pelvis (a seemingly appropriate surrogate) versus 25% in the WART arm (9). Similarly, another RCT of chemotherapy versus radiation therapy, which included 30% early stage, high-risk endometrial cancer patients, reported an increase in the incidence of local recurrences in the chemotherapy arm (7). Retrospective studies have also reported an increase risk of pelvic recurrences in high-risk endometrial cancer patients treated with chemotherapy alone (8). Although chemotherapy treatment in early stage, high-risk and advanced stage endometrial cancer patients appears to carry an increased risk for locoregional recurrences, the increased risk for locoregional recurrence may be diminished with the use of adjuvant whole-pelvic radiation therapy. There is increasing interest in a combined approach of chemotherapy plus radiation therapy for the treatment of high-risk endometrial cancer patients. Fields et al. recently reported on a phase II trial investigating pelvic radiation "sandwiched" between six cycles of chemotherapy (paclitaxel/platinum) (11). Although the cohort of patients was comprised of optimally reduced uterine papillary serous carcinoma, bone metastases were reported in 33% (1 of 30) of patients. The location of the bone metastasis was not given. A prospective Canadian trial of 33 patients with advanced stage endometrial cancer described a 30% incidence in bone metastases following "sandwich" therapy consisting of 4 cycles of paclitaxel and carboplatin followed sequentially with external beam RT and then an additional two cycles of chemotherapy (12). However, a randomized study of surgically staged high-risk endometrial cancer patients (Stage IA-B Grade 3 or Stage IC-IIIA) failed to demonstrate a significant difference in locoregional recurrence among patients randomized to adjuvant radiotherapy versus sequential chemo-radiotherapy (13).

Obviously, this patient offers a puzzling and unexpected outcome compared to treatment outcomes of other early stage, high-risk endometrial cancer patients. Because of the rarity of bone metastases in endometrial cancer patients and the heterogeneity in study cohorts and treatments, it is difficult to draw any meaningful conclusions about prognostic factors or treatment failure patterns that may identify patients that could be at an increased risk for pelvic bone metastases or locoregional recurrences. It is also unclear if the delay in the delivery of radiation therapy during the completion of the initial chemotherapy affects the outcome of endometrial cancer patients. The impact of sequential chemotherapy and radiation therapy on endometrial cancer outcomes may be best determined in a prospective fashion. Therefore, we eagerly await the completion of the PORTEC-3 trial, which may help determine if treatment failures (specifically pelvic bone metastases and locoregional recurrences) are truly associated with sequential chemotherapy and radiation therapy treatments for early stage, high-risk endometrial cancer patients.

Conflict of interest

We declare no conflicts of interest.

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