

Endometrial cancer recurrence in the sacrum and the Psoas: A case report and literature review

Judy Hayek^{a,*}, Rishika Reddy^a, Gary Goldberg^b, Ioannis Alagkiozidis^a

^a Zucker School of Medicine at Hofstra/Northwell Health at Staten Island University Hospital, United States

^b Zucker School of Medicine at Hofstra/Northwell Health at Long Island Jewish, United States

ARTICLE INFO

Keywords:

Recurrence
Endometrial cancer
Sacrum
Psoas
Chemotherapy
Radiation

ABSTRACT

Musculoskeletal metastasis of endometrial carcinoma is rare. Data regarding the management of metastatic disease to these sites is limited. We report a case of a 73-year-old woman who had surgery for endometrial adenocarcinoma (FIGO stage IB, Grade II) followed by vaginal cuff brachytherapy and one year later developed an isolated recurrence in the sacrum and iliopsoas muscle. She was treated with chemotherapy followed by whole pelvis radiation and a complete clinical response was achieved. At her last follow up, 12 months after the completion of the radiation, she had no clinical or radiologic evidence of disease.

1. Introduction/Background

Endometrial cancer is the fourth most common cancer among women in the U.S. and the most frequently diagnosed gynecologic malignancy. Multiple theories have been proposed to explain the pattern of metastasis of endometrial cancer. It has been shown to spread through direct extension, *trans*-tubal passage, lymphatic drainage, and hematogenous dissemination. Usual sites of metastasis include the cervix, parametria, pelvic and paraaortic lymph nodes. Unusual metastatic sites include the lungs, liver, bones and brain. Bone involvement specifically, occurs in less than 15% of all patients with metastatic disease. Isolated muscle metastasis has rarely been described. We present a case of a woman diagnosed with high-intermediate risk endometrial cancer that developed a recurrence in the sacrum and iliopsoas muscle. We document the diagnosis, treatment and outcome and review the literature on musculoskeletal metastasis of endometrial cancer. The results of our literature review are provided in [Table 1](#).

2. Case report

A written informed consent was obtained from patient. A 73-year-old woman (para 2) presented with postmenopausal bleeding for one year. An office endometrial biopsy revealed endometrial adenocarcinoma, grade 2 with possible serous features. Pre-operative imaging showed no evidence of metastatic disease. She underwent a total laparoscopic hysterectomy, bilateral salpingo-oophorectomy and sentinel lymph

node dissection in November 2017. The final pathology showed an endometrioid endometrial adenocarcinoma, FIGO Grade II with myometrial invasion to a depth of 60%. Lympho-vascular space invasion (LVSI) was present. She received adjuvant vaginal cuff brachytherapy (VCB) at 2100 cGy. Eleven months after completion of the adjuvant therapy, she reported new onset of left lower extremity pain and swelling, as well as hip pain. Magnetic Resonance Imaging (MRI) showed a large (5.1 × 5.6 cm) complex soft tissue mass in the left upper pelvic sidewall displacing the iliopsoas musculature overlying the sacroiliac articulation tapering at the level of the ischium with a rim enhancing cystic component with slight nodularity. On positron emission tomography-CT (PET-CT), the mass appeared to be hypermetabolic ([Image 1](#)). CT guided biopsy revealed metastatic endometrioid adenocarcinoma. The mass was determined to be surgically unresectable. Given the size of the mass, it was considered that complete response could not be achieved with radiation alone. She received six cycles of IV carboplatin and paclitaxel and repeat imaging showed a good clinical response with significant decrease in size. She continued with a course of whole pelvis radiation (4500 cGy) that resulted in a complete clinical response. She remains disease free 12 months after the completion of radiation and chemotherapy.

3. Discussion

Musculoskeletal metastasis of gynecological cancers has been described in women mostly with cancer of the cervix and the psoas

* Corresponding author: 52 Cheever Place, Brooklyn, NY 11231, United States.

E-mail address: jhayek@northwell.edu (J. Hayek).

<https://doi.org/10.1016/j.gore.2021.100814>

Received 20 April 2021; Received in revised form 14 June 2021; Accepted 16 June 2021

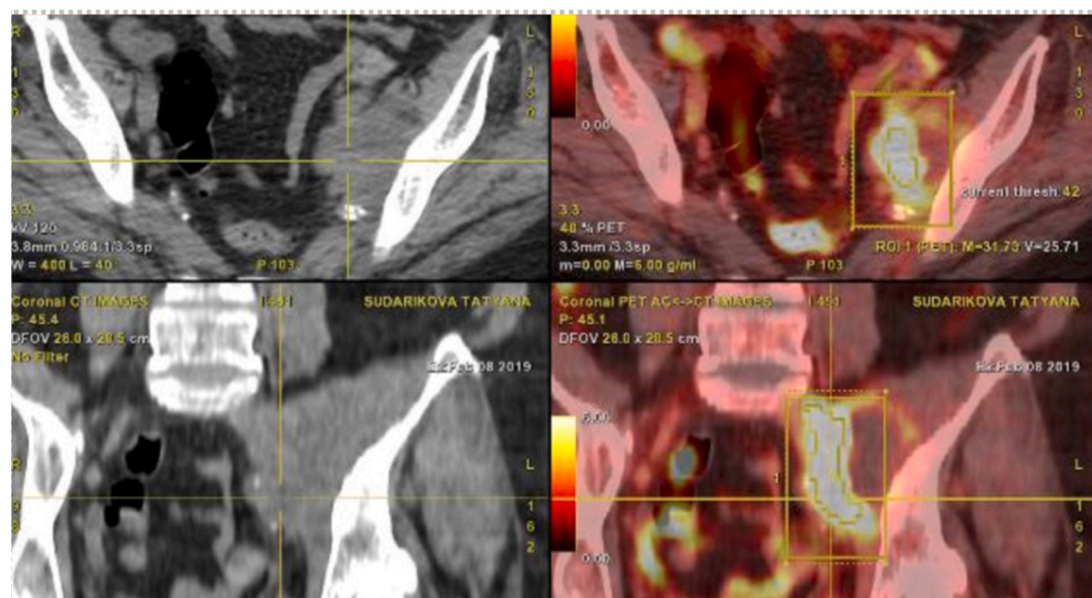
Available online 19 June 2021

2352-5789/© 2021 Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Table 1

Case Reports of metastases to the musculoskeletal system.

Study	FIGO Stage	Histology	Initial treatment	Site of recurrence	Treatment of recurrence
Albareda et al.	stage IB	Grade I endometrial adenocarcinoma		Sacrum	Surgical resection
Gunsu et al.	Stage IB	Grade I endometroid	Surgical & EBRT	Femur, vertebra and costa	Cisplatin + Epirubicin
	Stage IB	Grade 3 Clear cell	Surgical & brachytherapy	Vertebra	Refused treatment
	Stage IB	Grade 2 Endometroid	Surgical & brachytherapy	Femur and tibia	Surgical + RT + arboptatin/paclitaxel
	Stage IB	Grade 2 endometroid	Surgical & brachytherapy	Femur, pelvis, costa and sternum	Unreported
	Stage IB	Grade 1 endometroid	Surgical	Pelvis	RT + carboplatin/paclitaxel + Megace
	Stage IIIC1	Grade 2 endometroid	Surgical, EBRT & chemotherapy	Vertebra and lung	RT
	Stage IIIC2	Grade 2 endometroid	Surgical & EBRT	Vertebra	RT
	Stage IIIC2	Grade 3 serous	Surgical & EBRT	Femur, brain, lung & abdomen	RT + carboplatin/paclitaxel
Khoo et al. Djurdjević et al.	Stage IIIC2	Grade 1 endometroid	Surgical, EBRT & chemotherapy	Not reported	Chemotherapy (protocol unreported)
	Stage IIIC2	Grade 3 undifferentiated	Surgical & chemotherapy	Femur, costa and sternum	RT
	unreported	unreported	Surgical & chemotherapy	Ileum and Sacrum	Unreported
	stage IIIA	unreported	Surgical, chemotherapy, EBRT & Brachytherapy	Rectus abdominis and the psoas muscles	Unreported

**Image 1.**

muscle is the most common site of metastasis (Ishidera et al., 2018). Uterine cancer metastasis has been theorized to commonly include parametria, pelvic and paraaortic lymph nodes and less commonly the lungs, liver, bones and brain. Musculoskeletal metastasis has been rarely described. In case reports in the past 10 years, most musculoskeletal metastases were described with widespread metastatic disease, and rarely as an isolated metastasis (Kimyon et al., 2016; Ho et al., 2010).

In a literature review, there was a case of sacral metastasis reported by Albareda et al. (2008). They describe a patient with FIGO stage IB grade I endometrial adenocarcinoma that developed a solitary recurrence in the sacrum that was amenable to surgical resection. In a study by Kimyon et al. (2016) bone recurrence was seen, via imaging, in 10 of 162 endometrial cancer recurrence cases who underwent primary surgical management with/without adjuvant therapy. The most common site was the femur followed by the vertebrae. Five patients had stage IB disease, one had stage IIIC1 and four had stage IIIC2. Khoo and Rashid (2017) also reported a case of ilio-sacral metastasis extending to the surrounding musculature 5 years after treatment with total abdominal hysterectomy and bilateral salpingo-oophorectomy followed by a course of chemotherapy, details were not specified in the report.

Similarly, a case of recurrent endometrial cancer to the rectus abdominis and the psoas muscles confirmed histologically upon surgical resection has been reported by Djurdjević et al. (2006). The recurrence timeline was not described; but the primary cancer was FIGO stage IIIA, and had been treated with primary surgery, external-beam whole pelvic radiation followed by intravaginal radiation and adjuvant chemotherapy with carboplatin/Adriamycin.

We report a case of a large recurrence involving both the sacrum and the psoas muscle that was not amenable to surgical resection. Sequential treatment with platinum-based chemotherapy followed by whole pelvic radiation was chosen for our patient. The rationale was that the tumor was chemotherapy naïve and a favorable response to chemotherapy that would downsize the tumor would be expected, followed by radiation to potentially eliminate the disease. The treatment was well tolerated, and a complete response was achieved.

Our patient was initially diagnosed with high intermediate risk endometrial cancer and she had VCB as adjuvant therapy. According to PORTEC 2, VCB is as effective as external beam radiation in prevention of vaginal recurrence, with fewer adverse effects and better quality of life (Nout et al., 2010). As a result of these data, VCB has been adopted as

the preferred form of adjuvant radiation for patients with high intermediate risk endometrial cancer. However, there was a trend for increased pelvic recurrences with VCB in PORTEC 2 and the data on management of pelvic failures is limited. Our case demonstrates that chemotherapy followed by definitive radiation can be an effective treatment plan for a patient with isolated bulky recurrence involving the bony pelvis.

Molecular classification has been of significant prognostic value in endometrial cancer. The primary tumor in our case was noted to be of focal serous features with aberrant expression of p53 and p16. Molecular studies obtained on the recurrent mass showed intact expression of MMR proteins and positivity for ER (strong) and Vimentin (focal). POLE mutation was not investigated. In the TransPORTEC initiative, the arm with P53 mutant had a 5-year disease free survival of 42% compared to 93%, and 95% in the arms that are POLE-mutant and microsatellite unstable, respectively ($p < 0.001$). In addition, P53 mutant arm had a 50% rate of distant metastasis compared to none in the other two arms ($p < 0.001$) (Stelloo et al., 2015). León-Castillo et al further investigated the utility of adjuvant chemotherapy for each molecular subgroup. The trial found that the 5-year recurrence-free survival with chemotherapy/radiotherapy versus radiotherapy for p53 mutant endometrial cancer was 59% versus 36% ($p = 0.019$) (León-Castillo et al., 2020).

Regarding the mechanism of dissemination of endometrial cancer cells to the sacrum and the psoas muscle, extra-nodal extension of resident occult disease in the lymph nodes or *trans*-tubal passage and peritoneal dissemination could be implicated. Hematogenous spread is less likely given the metastatic lymphatic pathways, peritoneal spread or direct extension of the disease.

Our case may closely resemble the Malignant Psoas Syndrome (MPS), which is an underrecognized continuum of signs and symptoms first described in 1990. It is characterized by painful flexion of the ipsilateral hip associated with evidence of malignant involvement of the ipsilateral psoas major muscle. In a recent literature review (Takamatsu et al., 2018), 39 cases of Malignant Psoas Syndrome were identified, and gynecological malignancies were the most common, followed by gastrointestinal and urinary tracts. Primary uterine cancer metastasis was described as the source of a few cases of MPS, but none have been described in the past 5 years. One case of a recurrent uterine metastasis to the psoas muscle was noted on CT imaging as *para*-aortic lymph node metastatic invasion. The primary tumor was stage IB endometrial serous adenocarcinoma that was treated with total abdominal hysterectomy, bilateral salpingo-oophorectomy and lymphadenectomy followed by adjuvant chemotherapy.

In conclusion, we present a case of a pelvic recurrence involving the sacrum and psoas muscle in a woman who had surgical staging procedure for endometrial cancer followed by vaginal cuff brachytherapy. Due to the size and location of the recurrent tumor, it was not amenable to complete surgical resection. Sequential treatment with systemic chemotherapy followed by external beam radiation resulted in a complete clinical response and she remains disease free >12 months.

CRediT authorship contribution statement

Judy Hayek: Investigation, Data curation, Writing - original draft, Visualization. **Rishika Reddy:** Investigation, Writing - original draft, Validation. **Gary Goldberg:** Writing - review & editing. **Ioannis Alagkiozidis:** Writing - review & editing, Supervision, Project administration.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

- Albareda, J., Herrera, M., Lopez Salva, A., Garcia Donas, J., Gonzalez, R., 2008. Sacral metastasis in a patient with endometrial cancer: case report and review of the literature. *Gynecol. Oncol.* 111 (3), 583–588. <https://doi.org/10.1016/j.ygyno.2008.04.005>. Epub 2008 May 22 PMID: 18501410.
- Djurđević, S., Mladenović-Segedi, L., Djolai, M., 2006. Endometrial cancer metastases in the region of abdominal muscles and pelvic wall. *J BUON* 11 (1), 75–78. PMID: 17318956 (endometrial adenocarcinoma recurrence to rectus A and psoas treated with surgery, chemo and radiation).
- Ho, Linh, Sheth, Sindu, Seto, John, 2010. Intramuscular metastasis of endometrial carcinoma on FDG PET/CT. *Clin. Nucl. Med.* 35 (8), 607–609. <https://doi.org/10.1097/RLU.0b013e3181e4dc6b>.
- Ishidera, Y., Yoshida, H., Oi, Y., Katayama, K., Ando, N., Shigetani, H., 2018. A case of uterine carcinosarcoma which was strongly suspected to have metastases to the psoas and gluteus muscles. *Int. Cancer Conf J.* 7 (4), 121–124. <https://doi.org/10.1007/s13691-018-0333-2>. PMID: 31149529; PMCID: PMC6498333.
- Khoo, A.C.H., Rashid, N.K.A., 2017. Recurrent endometrioid adenocarcinoma of endometrium with bone metastases. *Clin. Nucl. Med.* 42 (8), 635–636. <https://doi.org/10.1097/RLU.0000000000001694>. PMID: 28481802.
- Kimyon, G., Karalok, A., Basaran, D., Ureyen, I., Celik, M., Tasci, T., Tulunay, G., Turan, T., 2016. Bone recurrence rarely seen in endometrial cancer and review of the literature. *J. Obstet. Gynaecol. Res.* 42 (6), 602–611. <https://doi.org/10.1111/jog.12960>. Epub 2016 Apr 13 PMID: 27074755.
- León-Castillo, A., de Boer, S.M., Powell, M.E., Mileskin, L.R., Mackay, H.J., Leary, A., Nijman, H.W., Singh, N., Pollock, P.M., Bessette, P., Fyles, A., Haie-Meder, C., Smit, V.T.H.B.M., Edmondson, R.J., Putter, H., Kitchener, H.C., Crosbie, E.J., de Bruyn, M., Nout, R.A., Horeweg, N., Creutzberg, C.L., Bosse, T., TransPORTEC consortium, 2020. Molecular classification of the PORTEC-3 trial for high-risk endometrial cancer: Impact on prognosis and benefit from adjuvant therapy. *J. Clin. Oncol.* 38 (29), 3388–3397. <https://doi.org/10.1200/JCO.20.00549>. Epub 2020 Aug 4. PMID: 32749941; PMCID: PMC7527156.
- Nout, R.A., Smit, V.T., Putter, H., Jürgenliemk-Schulz, I.M., Jobsen, J.J., Lutgens, L.C., van der Steen-Banasik, E.M., Mens, J.W., Slot, A., Kroese, M.C., van Bunnigen, B.N., Ansink, A.C., van Putten, W.L., Creutzberg, C.L., 2010. PORTEC Study Group. Vaginal brachytherapy versus pelvic external beam radiotherapy for patients with endometrial cancer of high-intermediate risk (PORTEC-2): an open-label, non-inferiority, randomised trial. *Lancet* 375 (9717), 816–823. [https://doi.org/10.1016/S0140-6736\(09\)62163-2](https://doi.org/10.1016/S0140-6736(09)62163-2). PMID: 20206777.
- Stelloo, E., Bosse, T., Nout, R.A., MacKay, H.J., Church, D.N., Nijman, H.W., Leary, A., Edmondson, R.J., Powell, M.E., Crosbie, E.J., Kitchener, H.C., Mileskin, L., Pollock, P.M., Smit, V.T., Creutzberg, C.L., 2015. Refining prognosis and identifying targetable pathways for high-risk endometrial cancer: a TransPORTEC initiative. *Mod Pathol.* 28 (6), 836–844. <https://doi.org/10.1038/modpathol.2015.43>. Epub 2015 Feb 27 PMID: 25720322.
- Takamatsu, S., Murakami, K., Takaya, H., et al., 2018. Malignant psoas syndrome associated with gynecological malignancy: Three case reports and a review of the literature. *Mol. Clin. Oncol.* 9 (1), 82–86. <https://doi.org/10.3892/mco.2018.1635>.