



Subcutaneous Metastasis of Cancer of the Endometrium: Case Report

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Abstract

Background: Cancer of the endometrium is the third most common gynecological cancer after cancer of the cervix and cancer of the ovary in Kenya. It is the most common gynecologic malignancy in the United States. The most common endometrial cancer type is endometrioid adenocarcinoma. It is mostly confined to the uterus and less aggressive. The natural history of epithelial corpus cancer includes 4 potential routes of metastasis: contiguous extension, hematogenous dissemination, lymphatic embolization, and exfoliation with intraperitoneal spread.

Case Presentation: A 45-year-old female, Para 5 + 0, presented to our gynecologic oncology clinic in July 2017. The patient was referred from a peripheral health facility for chemotherapy following radical hysterectomy in May 2017 for endometrial cancer. Histology results of the specimen taken during surgery showed endometrial Ca stage 2, grade 3. The patient developed a swelling on the right leg after completion of 6 cycles of Carboplatin and Paclitaxel. The swelling was progressively increasing in size; reaching 7 cm over a period of 6 months. Biopsy specimen was taken from the swelling and histology showed features consistent with metastatic endometrioid adenocarcinoma.

Conclusion: This is a rare occurrence of distant metastasis of cancer of the endometrium. We recommend histologic evaluation of subcutaneous masses developing in patients with advanced endometrial cancer.

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Introduction

Cancer of the endometrium is the 3rd most common gynecological cancer after cancer of the cervix and cancer of the ovary at Moi Teaching and Referral hospital, Kenya. It is the most common gynecologic malignancy in the United States. The most common endometrial cancer type is endometrioid adenocarcinoma. It is confined to the uterus and less aggressive [1]. Serous, clear cell and Grade 3 histological types are more aggressive and likely to metastasize. The mode of spread is mainly lymphatic. It spreads from the pelvis to other scalene nodes [2]. Hematogenous spread is less common and it occurs in the lungs, brain, liver and bones [3].

The main mode of treatment of cancer of the endometrium is total abdominal hysterectomy and bilateral salpingo-oophrectomy with or without pelvic node dissection followed by radiotherapy in most cases [4].

Subcutaneous metastasis is unusual sites of metastasis for endometrial cancer. Most of the musculoskeletal metastasis as indicated in published case reports are mainly bone metastasis. A historic study on dissemination of endometrial cancer noted 6 cases (2.3%) of bone metastasis in 266 women [5]. The most common site of metastasis was the axial skeletal which involved 5 of the 6 (83%) of the patients. It is not clear whether the osseous spread in the 6 patients was the primary site of disease recurrence.

The common sites of recurrence of cancer of endometrium include bones, liver, lungs and the lymphatic system. Some of the rare areas of metastasis documented are the skin, breast, kidney and the heart. Skin and subcutaneous metastasis are rare and are mostly reported in cancer of the lung [6,7]. Few cases of cutaneous and subcutaneous metastasis from cancer of endometrium have been reported in the literature [6,8,9].



Figure 1: Right pretibial area of the right leg showing the swelling of about 7 cm.

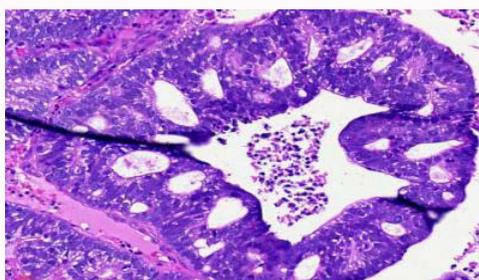


Figure 2: Crowded back to back endometrial-type neoplastic glands.

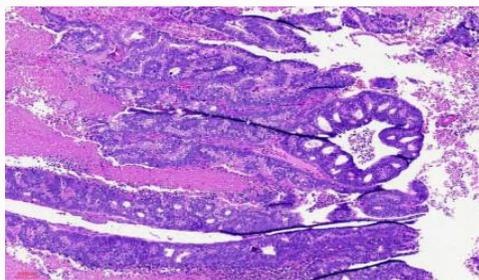


Figure 3: Glandular tumor with irregular glands, minimal intervening stroma and tumor necrosis.

Main areas of cutaneous and subcutaneous metastasis are Abdominal, perineal surfaces, skin and toes [6,10].

Case Presentation

A 45-year-old female, Para 5 + 0, presented to our gynecologic oncology clinic at Moi Teaching and Referral Hospital in July 2017 as a referral from a peripheral hospital where she underwent radical hysterectomy for endometrial adenocarcinoma in May 2017. Following radical hysterectomy, histology was reported as endometrioid adenocarcinoma stage 2A, FIGO grade 3. The patient was referred to our gynecologic oncology unit for adjuvant chemotherapy. She received 6 cycles of carboplatin and paclitaxel. The patient developed a swelling on the right leg following completion of chemotherapy. The swelling increased in size to a diameter of 7 cm over a period of 6 months. The swelling was warm, shiny, smooth and tender (Figure 1).

The patient remained in fair general condition, without any palpable nodes. Her vitals remained stable. All the other systems were essentially normal on examination. The baseline laboratory investigations such as complete blood count and renal function tests were normal. X-ray of the lower limb queried Myositis/Osteomyelitis. CT scan of the abdomen and pelvis showed a focal right liver lobe

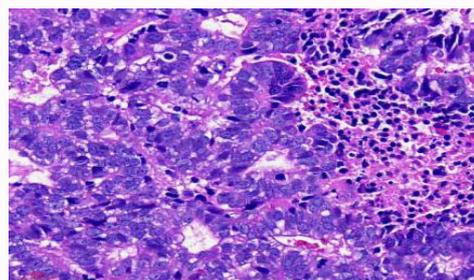


Figure 4: The cells with moderate to severe nuclear atypia.

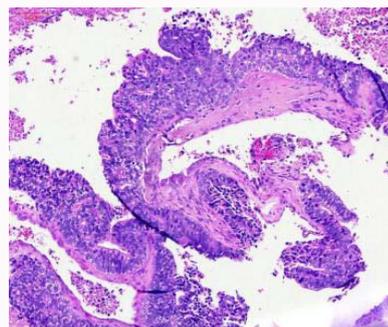


Figure 5: Neoplastic cellular tumor with angiolympathic invasion.

hypodense nodule about 1.5 cm. Other parameters of abdominal-pelvic CT scan were normal.

An excision biopsy was taken from the leg swelling for histologic examination. Microscopically, sections from the leg mass showed a tumor composed of pleomorphic epithelial cells forming irregular, crowded, back to back endometrial-type glands with minimal intervening stroma (Figure 2). The tumor cells exhibited moderate to severe nuclear atypia and pale, eosinophilic cytoplasm (Figure 4). Tumor necrosis was prominent (Figure 3). Angiolympathic invasion was noted (Figure 5). These features were consistent with metastatic endometrioid adenocarcinoma.

The Patient was started on Pegylated Liposomal Doxorubicin. Local radiation of the metastatic subcutaneous lesion was also done. Orthopedic consult confirmed no bone involvement. In view of the metastasis to the lungs, the patient was started on palliative care. However, the patient succumbed in to metastatic endometrial cancer in August 2018.

Discussion

We present a case of a patient who was on follow up for cancer of the endometrium who underwent adjuvant chemotherapy after radical hysterectomy and presented with pretibial subcutaneous metastasis. Although the standard care is administration of radiotherapy following a course of chemotherapy to prevent vaginal vault recurrences, this patient didn't receive radiotherapy after chemotherapy. This is because radiotherapy services are not available in our setting. It is unclear whether subcutaneous metastasis in this patient should be attributed to the omission of radiotherapy in her management.

The use of radiation therapy for endometrial cancer has been widely evaluated in randomized and retrospective series but still remains controversial in some stages [11-13]. According to Aalders et al., the addition of external beam irradiation after total abdominal

hysterectomy and Bilateral Salpingo-oophorectomy and vaginal brachytherapy led to a reduction in vaginal and pelvic recurrence rate; although the findings were not statistically significant [11].

According to PORTEC studies, radiation reduces vault recurrence [2,14]. However, our patient did not receive radiotherapy due to unavailability of the service. Portec I trial showed significant locoregional benefit with radiotherapy. Postoperative pelvic radiotherapy was indicated for patients over the age of 60, with grade 3 endometrial cancer or those with endometrial cancer with >50% myometrial invasion [15].

The PORTEC 2 trial had shown that brachytherapy should be the adjuvant treatment for patients with endometrial cancer in the high intermediate risk group [14]. According to PORTEC 3 trial adjuvant chemotherapy given during and after radiotherapy for high risk endometrial cancer did not improve overall 5-year survival although it increased failure free survival [2].

Distant metastasis poses a challenge in management. In our case, this called for multidisciplinary approach involving the orthopedic surgeons and the radiation oncologist. The Orthopedic surgeons confirmed the tumor was limited to the subcutaneous tissue and there was no bone involvement as previously thought from the clinical examination.

The management of this patient involved local radiation. This is in agreement with some studies that advocate for conformational radiation of the specific recurrences of certain organs for Stereotactic Body Radiation therapy (SBRT). SBRT has been shown to have advantages over conventional radiotherapy in being able to deliver higher doses while minimizing normal tissue radiation exposure. The tumor receives a higher biologically equivalent dose than the conventional radiation [16].

Separate series describing the use of stereotactic radiosurgery for distant or local recurrences of endometrial and cervical cancer have been described in the literature [17,18]. In these studies, favorable rates of local control were illustrated although the statistics for cervical and uterine cancer were not reported separately.

Conclusion

This is rare occurrence of distant metastasis of cancer of the endometrium. We recommend histologic evaluation of subcutaneous masses developing in patients with advanced endometrial cancer.

Ethical Considerations

The study was approved by the Moi University/Moi Teaching and Referral Hospital Institutional Research and Ethics Committee (IREC). The approval number is 0003167. A written informed consent was obtained from the patient (prior to her demise) before the study was conducted.

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