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Case report

Metastatic papillary serous uterine cancer presenting as a rash

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ABSTRACT

Background: We report diagnosis and management of stage IV papillary serous uterine cancer with initial clinical presentation as a skin rash.
Case: A 62-year-old postmenopausal female developed an erythematous rash beginning on her right lower abdomen and progressively spreading to her left abdomen, vulva, and neck. After a trial of antibiotic treatment, biopsy of left neck and right thigh skin nodules revealed papillary serous carcinoma. Abdominopelvic tomography revealed endometrial thickening and a 5 cm left adnexal mass. Subsequent endometrial biopsy also revealed papillary serous carcinoma, with pathology similar to that of the skin lesions. She received 6 cycles of carboplatin and paclitaxel chemotherapy with improvement of her skin lesions and overall performance status. However, her CA-125 level continued to rise and she was treated with single-agent carboplatin with progression of both her internal and cutaneous disease. She was transitioned to hospice with palliative radiation and died 2 months after discontinuing chemotherapy, 10 months after presentation.
Conclusion: Cutaneous metastasis is a rare presentation of metastatic uterine cancer. Treatment with chemotherapy may result in a positive response and should be considered.

1. Introduction

Uterine papillary serous cancer (UPSC) is a type II uterine cancer generally associated with more aggressive clinical behavior than type I or endometrioid cancer. Although type II cancers comprise 10–20% of endometrial cancer cases, they account for 40% of uterine cancer deaths (Moore and Fader, 2011). Abnormal uterine or postmenopausal bleeding are the most common presentation of both papillary serous and endometrioid uterine cancer (Keeble et al., 2014). Cutaneous metastasis of uterine cancer has been documented in the literature and is a rare occurrence. Our literature review revealed 10 reported cases of uterine cancer with metastasis to the skin over a 36-year period (Rasbach et al., 1978; Damewood et al., 1980; Debois, 1982; Espinos et al., 1992; Spencer et al., 1994; Kushner et al., 1997; La Fianza et al., 1998; Atallah et al., 2014; Elit et al., 2001; Kim et al., 2005). In all of these previous reports, the diagnosis of uterine cancer preceded the development of cutaneous metastases, which were late events. We report the case of a woman who presented with an abdominal rash found to represent stage IV UPSC, whose clinical course can provide a basis for discussing treatment options in this rare presentation.

2. Case

A 62-year-old gravida 2 para 2 postmenopausal female with a history of endometriosis and early menopause at 33 years of age presented to the emergency department with a new-onset groin rash, genital pain, and dysuria. She denied any other gynecologic symptoms including abnormal vaginal discharge and postmenopausal bleeding. At that time, she reported recently moving into a new home with contaminated water which stained her clothes. Approximately 3 weeks after moving she developed an erythematous rash on her right lower abdomen which progressively spread to her groin and vulva. She noted the development of papules and bullous lesions as the rash progressed and noted the development of a single papule on her left neck. Her primary care provider prescribed oral clindamycin for the rash but noted worsening of the rash despite antibiotic treatment. Of note, she experienced an unintentional weight loss of 40 lb in the last 6 months. At initial presentation to our emergency department, physical exam was significant for labial induration with a tender 2 cm vesicular lesion with fibrinous exudates (Fig. 1a), an erythematous maculopapular rash extending from the inferior abdomen to the groin (Fig. 1b), and several nodular lesions scattered throughout the perineum. Internal gynecologic examination revealed a cervix that was bulky at 3–4 cm but without a visible lesion, and the uterus was enlarged to 12–14 weeks size, with no evidence of parametrial thickening. A computerized tomography (CT) scan was performed which revealed abnormally enhancing and thickened right labial fold, and morphologically abnormal and enlarged inguinal lymph

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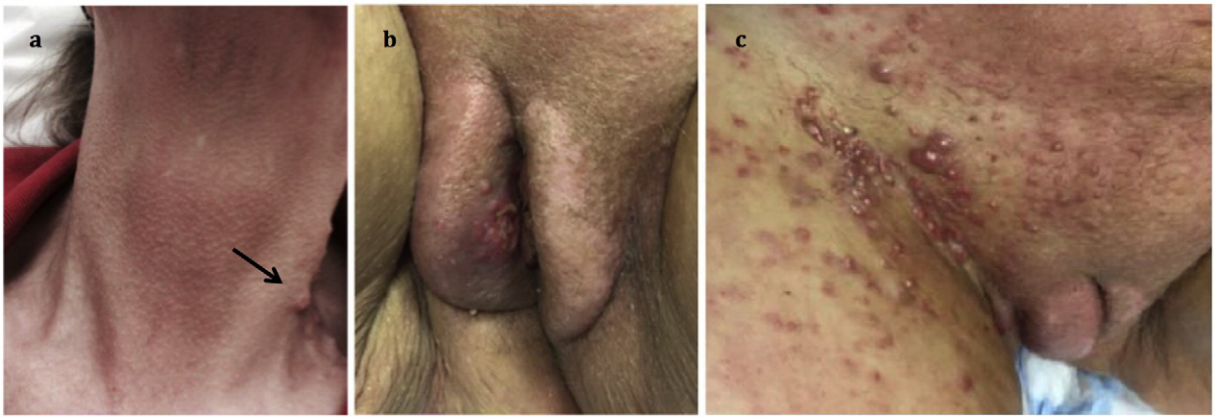

Fig. 1. a: Papular neck left lesion. b: Labial induration with a tender 2 cm vesicular lesion with fibrinous exudates. c: Erythematous maculopapular rash extending from the inferior abdomen to the groin.

nodes. The patient was eager to leave the emergency department and refused further evaluation at the time. As such, a complete evaluation was unable to be performed. Given concern for superimposed infection, a herpes simplex virus culture was obtained from one of the labial lesions and she was started on empiric antibiotics for a 10 day course and scheduled to return for a follow up in our outpatient gynecology and dermatology clinics.

At the patient's outpatient follow up, she reported no improvement of her rash or labial pain despite the antibiotics. Herpes simplex virus culture obtained from her prior emergency department visit returned positive and patient was prescribed valcyclovir for treatment of presumed outbreak but this diagnosis did not provide an explanation for her systemic findings. A pelvic ultrasound was performed and revealed a uterine body measuring 7.0 cm by 4.6 cm × 5.4 cm with a thickened endometrial stripe heterogeneous and difficult to differentiate from surrounding myometrium. An endometrial biopsy was performed and revealed fragments of markedly atypical epithelium favoring papillary serous carcinoma (Fig. 2a). A shave biopsy of a left neck lesion and punch biopsy of the right thigh lesion revealed metastatic papillary serous carcinoma consistent with mullerian primary origin (Fig. 2b). The patient was subsequently referred to our gynecologic oncology service for further management.

Given the widely metastatic nature of her disease, she was started on carboplatin/paclitaxel and completed 6 cycles of chemotherapy. Serial physical exams showed resolution of rash consistent with treatment response (Fig. 3). CA-125 levels were trended throughout her treatment course and was 174 U/mL at the conclusion of 6 cycles of chemotherapy. After 6 cycles, CT imaging of her chest, abdomen, and pelvis was performed and revealed suspicious nodules in her right lung and axilla in addition to interval resolution of inguinal adenopathy, significant reduction in size of a left adnexal mass, and decreased volume of the uterus. It is unclear if the right pulmonary and axillary nodules represent progressive disease or were present initially given a chest CT was not performed when she initially presented. Given the appearance of a positive response, consideration was given to surgery with hysterectomy and debulking, but the extent of initial disease raised concern that the procedure would not remove all residual disease and not be curative. Additionally the patient did not feel her performance status to be adequate to undergo surgery. A chemotherapy holiday was initiated with a plan to reevaluate in 2 months. However, the patient returned approximately 1 month after completion of her chemotherapy reporting recurrence of skin lesions. Additionally her CA-125 increased to 624 U/mL. She was started on single-agent carboplatin given her prior response to treatment and received 1 cycle prior to rapid progression of disease. She began to have vaginal bleeding and was referred to radiation oncology for consideration of palliative radiation treatment where she received external beam radiation therapy to a dose of 16 Gy in 2 fractions. The patient was offered additional chemotherapy, but with the low likelihood of a response given rapid regrowth, she requested transition to hospice care. She had continued deterioration of functional status and died 2 months after discontinuing chemotherapy treatment.

3. Discussion

In this case, we described the diagnosis and management of a woman with stage IV UPSC and cutaneous metastasis. This case is unique in that the initial presentation of the disease was her skin lesions. It may be helpful to the community to know that although she had disseminated disease, she had a positive initial response to chemotherapy, and therefore treatment is a reasonable option. However, consistent with her poor prognosis, the patient experienced a rapid recurrence, decline, and death.

Although most early uterine cancer patients will have vaginal bleeding, some may have none. On initial presentation, this patient made it

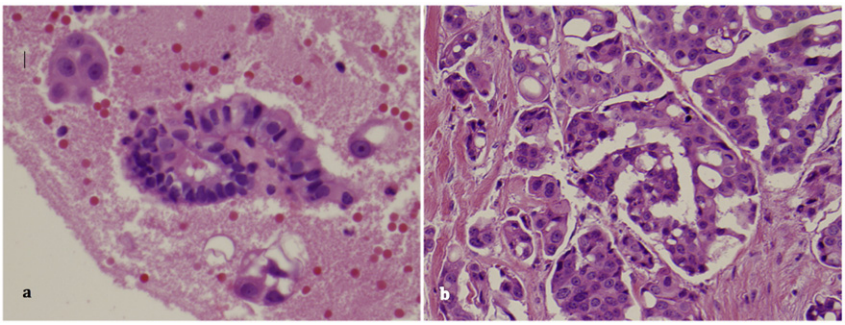

Fig. 2. a: Hematoxylin and eosin stain of endometrial biopsy revealing fragments of markedly atypical epithelium favoring serous carcinoma. b: Hematoxylin and eosin stain of biopsied right thigh skin lesion revealing similar pathologic findings from endometrial biopsy suggestive of metastatic serous carcinoma.

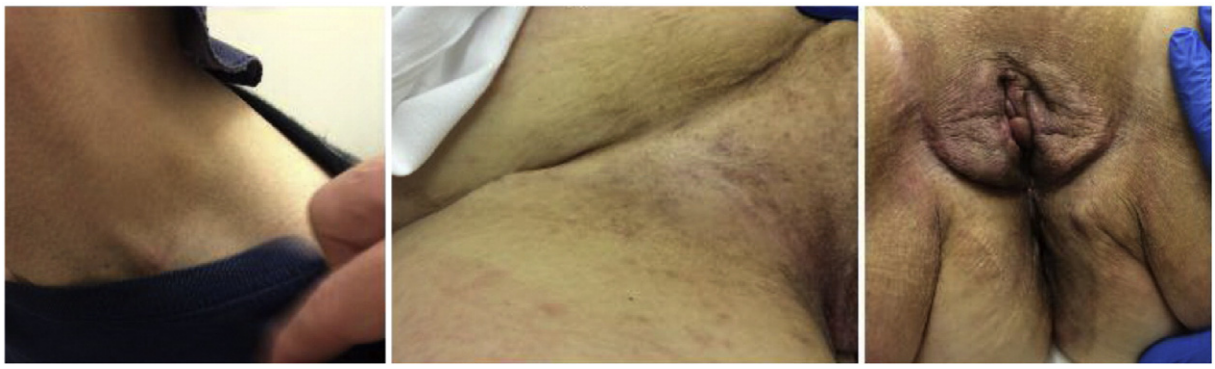

Fig. 3. Nearly complete resolution of skin lesions after 6 cycles of treatment with carboplatin and paclitaxel.

known that she had not experienced any vaginal bleeding since becoming menopausal. Prior to her workup, the differential for her skin lesions was extensive and included contact dermatitis, infection, autoimmune disorder, and malignancy. Importantly, there was no clear indication on initial presentation that this patient's skin lesions were a cutaneous manifestation of internal malignancy, specifically papillary serous uterine cancer. For this patient, gynecology was initially consulted out of concern for gynecologic infection. Clues that an underlying malignancy was present emerged with further evaluation and included the patient's unintentional weight loss of 40 lbs. over the last 6 weeks, bulky cervix, enlarged uterus, and CT findings. Finally, biopsy of the skin lesions with comparison to an endometrial biopsy allowed for a definitive diagnosis of metastatic serous carcinoma. This highlights that any patient with an aggressive cancer and unusual cutaneous lesions should have such lesions biopsied.

Many different presentations of cutaneous metastases of internal malignancy have been described. Our patient presented with a pattern of skin lesions and erythematous, inflammatory-appearing skin patches consistent with carcinoma erysipelatoides. This presentation is commonly mistaken for infection and treated as such. In such cases, delay in diagnosis oftentimes results in delay of effective treatment. Carcinoma erysipeloides most commonly occurs near the primary tumor and can involve firm, mobile nodules, indurated scar-like plaques from cancer cells infiltrating collagen, and carcinoma telangiectoides secondary to cancer cells infiltrating blood or lymphatic vessels. Diagnosis of carcinoma erysipeloides generally requires a biopsy of the involved skin, and histopathology of the biopsy will reveal malignant cells within the cutaneous lymphatics.

Cytotoxic chemotherapy is the primary treatment modality of metastatic uterine cancer with platinum-containing compounds, taxanes, and anthracyclines being the most commonly utilized agents. The combination of carboplatin and paclitaxel has been shown to demonstrate an overall response rate of over 60% with median overall survival of 15–26 months (Humber et al., 2007). In our patient, this regimen resulted in a dramatic improvement in her cutaneous disease, and in overall tumor burden as evidenced by imaging and CA-125 levels.

Although uterine cancer is the most common gynecologic cancer in the developed world, skin metastasis is rare with an estimated prevalence of 0.8% (Lerner et al., 1999). Skin metastases of uterine cancer has been described in the literature with a minority of cases involving serous histology, and with all described cases identifying skin metastasis after primary disease had been identified (Rasbach et al., 1978; Damewood et al., 1980; Debois, 1982; Espinos et al., 1992; Spencer et al., 1994; Kushner et al., 1997; La Fianza et al., 1998; Atallah et al., 2014). To our knowledge, however, skin metastasis as the initial presenting symptom of uterine cancer has not been reported and highlights the fact that this rare presentation may occur in the absence of all other common presenting signs or symptoms of uterine cancer. The case also demonstrates that a positive response to chemotherapy is possible and, despite the poor prognosis of stage IV uterine cancer, should be considered. In summary, the skin is an exceedingly rare site of metastasis of uterine cancer and it is important for the clinician to recognize that metastatic uterine cancer can clinically present as skin lesions.

Disclosure summary

The authors have nothing to disclose.

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