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Case report

Delayed and clinically isolated port site carcinosarcoma recurrence as an early indicator of disseminated disease

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ABSTRACT

A 71-year-old woman with suspected endometrial cancer underwent robotic-assisted hysterectomy, bilateral salpingo-oophorectomy, pelvic and para-aortic lymph node dissection, and infracolic omentectomy revealing a stage II uterine carcinosarcoma with components of serous adenocarcinoma and undifferentiated spindle cell sarcoma. There was no evidence of distant metastasis at the time of surgery. However pelvic washings were positive for malignant cells. She received adjuvant chemotherapy and vaginal cuff brachytherapy. Forty months later she developed a subcutaneous mass at the location of previous port site which was confirmed to be recurrence of the uterine primary. She subsequently developed additional distant metastases to the abdominal wall, lungs, and bone. Port site metastasis (PSM) was the earliest indicator of disseminated metastatic disease in this patient. We review challenges in the management of patients with PSM and propose that PSM be considered as a sign of systemic disease even when presenting as an apparently isolated recurrence.

1. Background

Minimally invasive gynecologic surgery (MIGS) for gynecologic malignancies was initially challenged regarding safety and efficacy. Discussions of port-site metastasis (PSM) questioned whether surgeon technical skill, port-site tumor extraction, local surgical seeding of port-sites, or pneumoperitoneum contributed to PSMs (Curet, 2004). The LAP2 trial reported a 0.24% (4/1696) PSM incidence (Walker et al., 2009, 2012). While uncommon, PSM remains troubling as some experts consider PSM indicative of advanced disease and poor prognosis (Zivanovic et al., 2008; Lönnerfors et al., 2013). Many PSMs are present in the setting of disseminated disease (Zivanovic et al., 2008; Lönnerfors et al., 2013). National Comprehensive Cancer Network guidelines recommend surgical excision of resectable, isolated metastases and consideration of adjuvant chemotherapy or radiation therapy (National Comprehensive Cancer Network, 2014). Therefore, administration of radiation or chemotherapy after surgical treatment of an isolated PSM is currently individualized based on expert opinion. Here we present an unusual case of a clinically isolated PSM diagnosed after a long 40 month disease free interval following MIGS staging of an early stage uterine carcinosarcoma. Ten months after management of the initial isolated PSM, the patient developed obvious disseminated disease. Apparently isolated PSM in this patient portended later development of disseminated disease. Increased reporting of outcomes associated with clinically isolated PSM may influence post-resection management by increasing utilization of systemic chemotherapy to treat suspected underlying disseminated disease.

2. Case

A 71 year old woman with body mass index of 21 kg/m^2 was presented with post-menopausal uterine bleeding and underwent endometrial biopsy, which revealed a high-grade endometrial serous adenocarcinoma. Computed tomography of the abdomen and pelvis demonstrated a 3.5 cm uterine mass, and was without evidence of lymphadenopathy, ascites, or metastasis.

Robotic-assisted total laparoscopic hysterectomy, bilateral salpingo-oophorectomy, pelvic and para-aortic lymph node dissection, and infracolic omentectomy was performed without complication. Five abdominal incisions were made for the robotic camera and instruments, as well as an accessory port. No adnexal masses were appreciated. The uterus was approximately 8-weeks in size. Electrocautery bilateral tubal ligation was first performed to prevent retrograde cancer cell spillage into the peritoneum. Pelvic and para-aortic lymphadenectomies were then performed. Next, bilateral salpingo-oophorectomy and hysterectomy were performed. The omentum appeared normal, and an infracolic omentectomy was performed. All surgical specimens were removed vaginally without difficulty. Port sites were closed

Abbreviations: PSM, port-site metastasis.

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using a GORE® suture passer and the skin was closed with 4–0 Vicryl. Incisions healed without complication. Pathologic diagnosis was stage II uterine carcinosarcoma with components of serous adenocarcinoma, endometrioid adenocarcinoma, undifferentiated carcinoma, and undifferentiated spindle cell sarcoma. The tumor was 2.5 cm in maximum dimension in the uterine fundus with maximum depth of invasion of 15% of total myometrial thickness and had superficial cervical stromal invasion. Cytology of pelvic washings was positive for malignant cells. She received adjuvant high-dose-rate vaginal cuff brachytherapy (2100 cGy total dose in 3 weekly fractions) between six cycles of paclitaxel (135 mg/m^2) and ifosfamide (1.6 g/m^2) every three weeks, with three cycles of chemotherapy administered before brachytherapy and an additional three cycles after brachytherapy.

She remained without evidence of disease for 40 months, when she presented with a subcutaneous mass on the right lower quadrant at the location of a previous port-site. Computed tomography of the abdomen and pelvis demonstrated a 3.5 cm heterogeneous mass in the deep subcutaneous tissues of the right lower quadrant and was without evidence of other disease (Fig. 1). She underwent surgical resection of the mass, which extended to the fascia but not the peritoneum, which was not entered. Margins were clear. Pathology confirmed metastasis (high grade adenocarcinoma) consistent with her previous uterine primary (Fig. 2). She received external beam radiotherapy of 5990 cGy total dose to the right lower quadrant recurrence site. She declined systemic chemotherapy. Five months later, she had a new palpable lump at the right flank, 3 cm superior to the previous mass. This recurrence developed in the previously radiated field. Positron emission tomography (PET/CT) was performed and revealed a solitary focus of activity in the superficial right abdominal wall distinct from the previous recurrence site (Fig. 3). The mass was resected with clean margins and pathology again confirmed metastasis consistent with the primary diagnosis.

In the presence of severe back pain, she underwent another PET/CT two months after resection, which revealed new pulmonary nodules concerning for metastasis and L4 vertebral metastasis. She began palliative oral etoposide (50 mg alternating with 100 mg for days 1–21, then 7 days off, every 28 days) chemotherapy. She is currently alive 53 months from initial diagnosis.

3. Discussion

Many hypotheses have been proposed to explain the development of PSM including direct wound seeding by specimen removal or contaminated instruments, aerosolization of exfoliated cancer cells, the "chimney effect" caused by insufflation, and pneumoperitoneum, carbon dioxide, or tissue trauma altering the normal immunologic defenses at port sites (Curet, 2004). There is little evidence to support any practice to reduce PSM risk (Curet, 2004). The LAP2 trial reported a low PSM incidence of 0.24%, which is acceptable compared to laparotomy (Walker et al., 2012; Gücer et al., 2005). Furthermore, the LAP2 trial

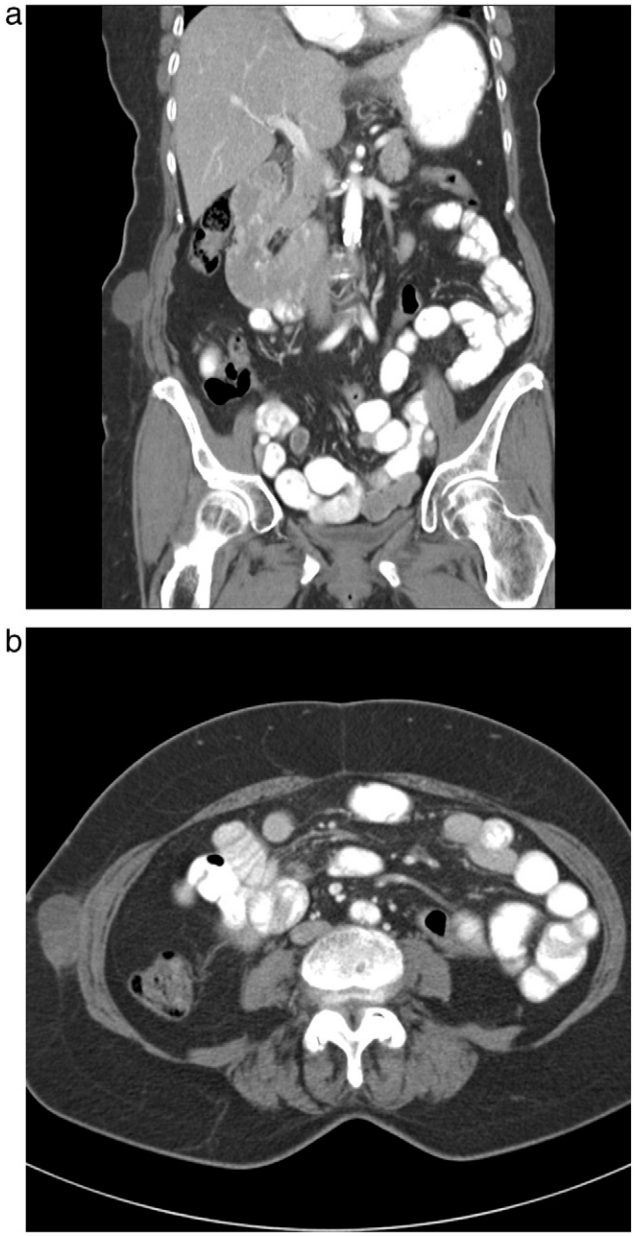

Fig. 1. CT abdomen/pelvis showing port-site recurrence.

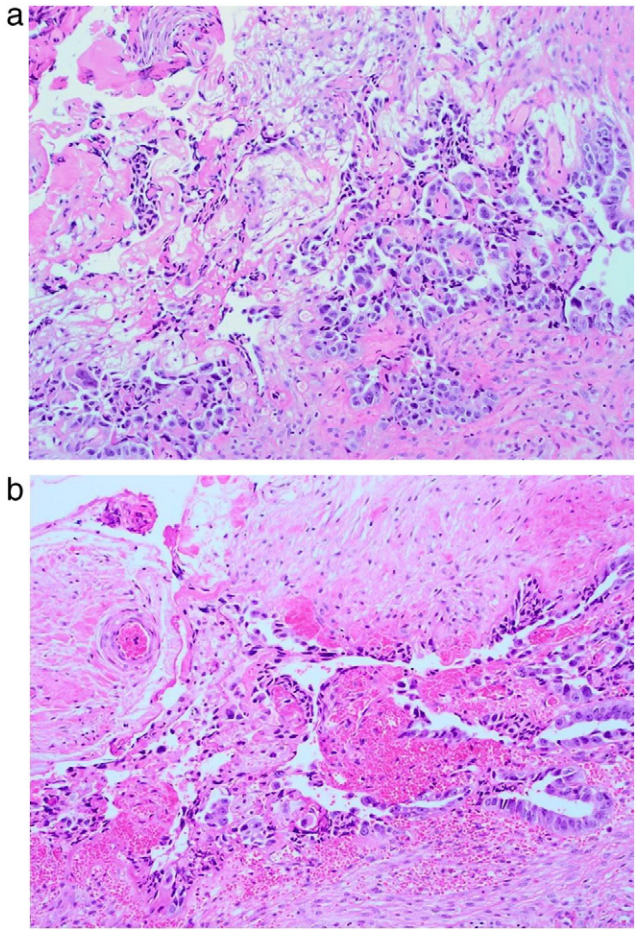

Fig. 2. Histology of PSM (100×) showing adenocarcinoma of primary tumor pathology.

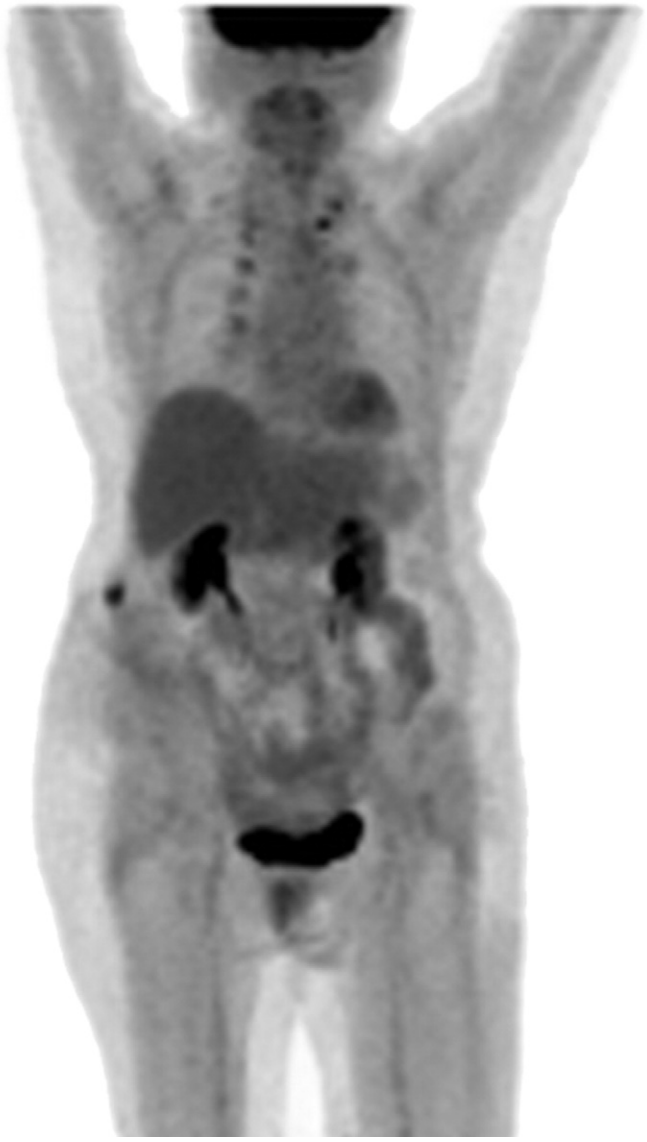

Fig. 3. PET/CT showing new recurrence at right flank abdominal wall, cephalic to location of previous PSM.

concluded that the use of MIS was safe regardless of pathological subtype (Walker et al., 2012).

Palomba et al. reviewed published data of PSM after staging for endometrial cancer (Palomba et al., 2012). PSM was isolated in 4 cases and developed with concurrent carcinomatosis in 8 cases. Isolated PSM were all endometrioid histology, high grade, and stage I or II at initial diagnosis. One patient declined excision and underwent palliative radiation plus hormone therapy before succumbing to disease 5 months later. One patient had excision followed by radiation and was disease free for 30 months before recurring and dying of disease 42 months after first recurrence. The other two patients had excision, radiation therapy and chemotherapy. Follow up data was unavailable for one patient. The second patient was disease free at 10 months after recurrence. Palomba et al. also concluded that apparently isolated PSM may represent occult, disseminated metastatic disease (Palomba et al., 2012).

Carlson et al. reported an interesting PSM at a right upper quadrant (RUQ) port-site used for laparoscopic cholecystectomy that was performed 6 months prior to the patient's staging and diagnosis of stage IIIC serous ovarian cancer (Carlson et al., 2002). Twenty-seven months after laparoscopic surgical staging and cytoreduction of the ovarian malignancy, she developed a PSM at a RUQ port-site from her prior laparoscopic cholecystectomy. The PSM was resected, and she was given platinum chemotherapy. Six months later she developed a pelvic recurrence and was treated with additional platinum chemotherapy. She subsequently remained disease free for three years prior to the report of her case. The apparently isolated RUQ PSM also preceded the development of additional metastatic disease despite treatment of the PSM with resection and systemic chemotherapy.

Uterine carcinosarcoma, although initially considered to be a sarcoma, is now recognized as an advanced carcinoma that undergoes an epithelial-to-mesenchymal transformation (Cantrell et al., 2015). It is one of the most aggressive types of uterine pathologies, associated with high recurrence rates and a 5-year survival of 33–39% (Cantrell et al., 2015). In our case, the patient developed an isolated uterine carcinosarcoma PSM after a 40 month disease free interval but before any indication of systemic disease. Later, she developed an additional abdominal wall metastasis, as well as suspected pulmonary and bone metastases. We believe that her PSM was an early indication of occult disseminated disease. We propose that when patients develop an apparently isolated PSM, although additional metastases may not yet be evident by imaging, the presence of PSM indicates high risk for progression of disease and warrants systemic treatment in additional to local excision and/or radiation. We propose that patients with apparently isolated PSM without evidence of other metastatic disease require systemic chemotherapy in addition to excision and/or radiation therapy to the site of recurrence. PSM of carcinosarcoma indicates a poor prognostic condition for the patient and palliative discussions should be initiated. Best management of isolated PSM is broadly relevant to Gynecologic Oncology practice. All patients undergoing laparoscopic surgery for cancer are at risk for PSM. Case reports, case series and literature reviews informing expert opinion will likely remain the highest level of evidence for the clinical dilemma of isolated PSM.

Conflict of interest statement

The authors declare that there are no conflicts of interest.

Disclaimer

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-In-Chief of this journal on request. This case report was exempt from IRB review.

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