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Cervical cancer with a rare umbilical metastases in prior surgical site

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ABSTRACT

INTRODUCTION: Port-site metastasis of cervical cancer is a relatively rare occurrence, and has been reported in the published literature as a pre-terminal event.
PRESENTATION OF CASE: We present the case of a 52-year-old female who was diagnosed with cervical cancer after presenting to our institution's hospital with urinary symptoms not relieved by multiple treatments with antibiotics. To fully evaluate the extent of disease, positron emission tomography-computed tomography imaging was obtained, showing an area of mildly increased fluorodeoxyglucose uptake in her umbilicus. While undergoing external-beam radiotherapy treatment for her cervical cancer, she began to experience pain in the umbilicus associated with a mass. A biopsy was taken, revealing metastatic cervical cancer at the site of a previous port-site incision for a cholecystectomy that the patient underwent 18 months before the finding.
DISCUSSION: Port-site metastasis have been reported following kidney, bladder, and colon cancer resections, with reports of cervical cancer cases being exceedingly rare. Several hypotheses have emerged as potential explanations for port-site metastasis.
CONCLUSION: To our knowledge, this represents the first reported case of a port-site metastasis to an incision site created for an unrelated laparoscopic surgery, performed well in advance of the diagnosis of cervical cancer.

1. Introduction

In developed countries, cervical cancer is the eleventh most common type of cancer in women, and ninth most common cause of cancer mortality [1]. Cervical cancer usually spreads through direct invasion of the surrounding anatomical structures or through the lymphatics and circulatory system. Hematogenous spread typically results in metastasis to the bones, lungs, and liver, while lymphatic spread travels first to the iliac, obturator, and then parametrial lymph nodes [2,3].

Imachi et al. reported a mean interval time between diagnosis of cervical cancer and discovery of skin metastasis of 16.9 months [4], with skin metastasis becoming more likely as the stage of cervical cancer increases [5]. Cutaneous metastasis from cervical cancer has previously been reported as a preterminal event, with a time of diagnosis to death of 3 months [6].

2. Presentation of case

A 52-year-old female was presented to our hospital's emergency department with a 6-week history of urinary incontinence, difficulty in initiating urination, and rectal pressure. She was previously treated with ciprofloxacin as an outpatient, but, despite treatment, her symptoms did not improve. On speculum examination, it appeared that the cervix was replaced with an exophytic tumor; on a subsequent speculum examination, the cervix measured about 6 cm with bilateral parametrial thickening.

A computed tomography (CT) scan of the abdomen and pelvis with intravenous contrast was obtained and showed a 5.8 × 5.7-cm enhancing mass in the cervix with involvement of the left parametrium and left ureter, causing mild hydronephrosis, with 2 left external iliac pathologic lymph nodes (Fig. 1). A papanicolaou test was also performed, revealing HPV 16 positivity, and, once discharged from the emergency department, an ectocervical biopsy was performed showing moderately differentiated invasive squamous cell carcinoma of the cervix (Fig. 2). This malignancy was determined to be stage IIIB T3b N1 M0 HPV-positive squamous cell carcinoma of the cervix. The patient underwent a positron emission tomography (PET)-CT in her staging workup that also demonstrated a focus of increased fluorodeoxyglucose uptake in the umbilicus. The radiologist noted it corresponded to an area of umbilical thickening measuring 2 cm (Fig. 3). They noted it may represent granulation tissue, previous infection, or even a tumor implant, though the latter seemed less likely. Correlation with history was recommended. Further questioning of the patient revealed that she previously had her gallbladder removed through the umbilicus; thus it was suggested that this was inflammation from scar

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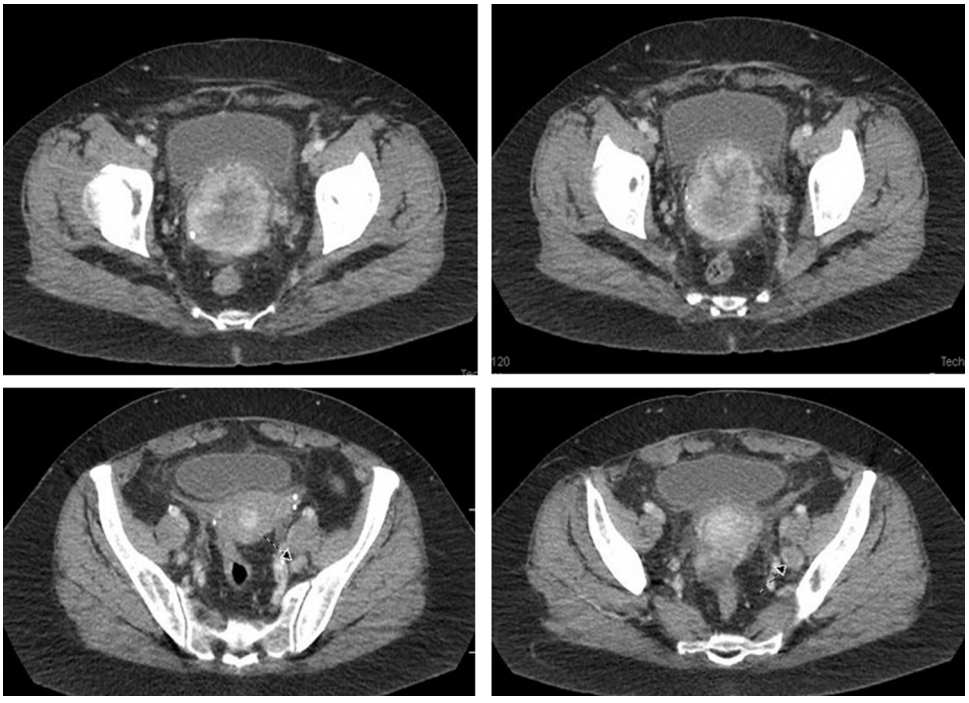

Fig. 1. The patient's pretreatment computed tomography (CT) scan. The top two images show the primary cervical mass. The bottom two images demonstrate the left external iliac lymphadenopathy.

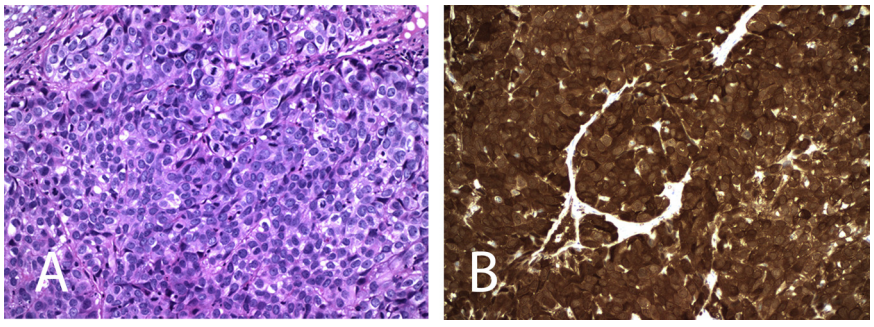

Fig. 2. (A) This histological section of the cervical tumor shows nests of infiltrating poorly-differentiated carcinoma cells with pleomorphic nuclei and cleared-out cytoplasm. Abundant mitoses and individual cell tumor necrosis is also noted. (B) The tumors cells were strongly and diffusely positive for the surrogate HPV marker, p16INK4a, as demonstrated by nuclear and cytoplasmic staining.

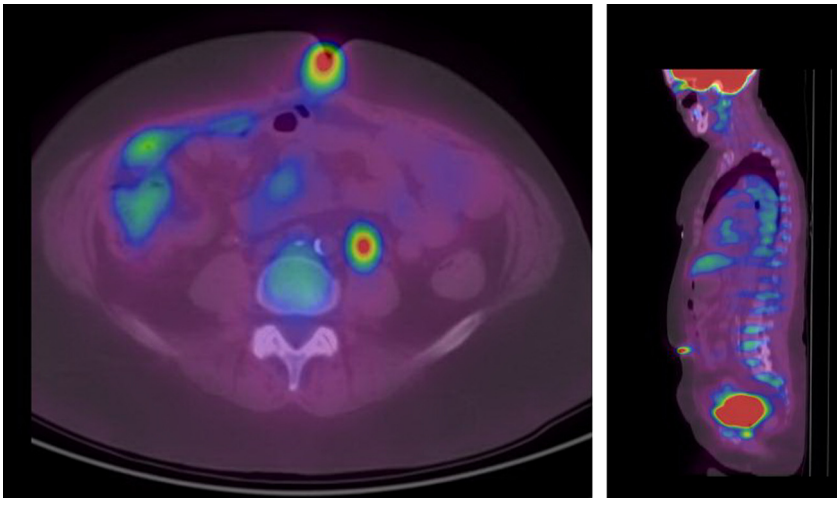

Fig. 3. These images demonstrate the positron emission tomography (PET) positivity of the umbilical mass in the anterior abdominal wall. The left one is the axial slice and the right one is the sagittal reconstruction.

tissue. The patient was evaluated by our department, and a plan was created to treat the entire pelvis with 45 Gy at 1.8 Gy/fraction, with a boost to the bilateral side walls and radiographically positive nodes to a total dose of 61.2 Gy over 34 fractions. She would be re-assessed for a brachytherapy boost after the fourth week of radiation. Also, she would undergo concurrent treatment with cisplatin with curative intent.

Four weeks after starting external-beam radiation therapy, the patient began experiencing periumbilical pain, which she attributed to a hernia. Due to the concerning finding on the previous PET scan showing uptake in the umbilicus, her case was presented at our gynecologic oncology tumor board. The consensus decision was to surgically remove this mass. A 3-cm nodule under the umbilicus involving the fascia was removed, and pathology revealed metastatic carcinoma consistent with poorly differentiated squamous carcinoma (Fig. 4). The entire specimen was sent for evaluation of the margins and the tumor was found to involve the inked deep margin. Immunohistochemistry was also performed to confirm the diagnosis and results showed the tumor was diffusely nuclear positive for p63 and strong nuclear and cytoplasmic positivity for p16, consistent with metastatic squamous cell carcinoma of cervical origin.

This resulted in up-staging of the cervical cancer to stage IVB T4b N1 M1, but she was already at the end of her definitive chemotherapy and radiation therapy, which she completed. The umbilical mass was found to be at the site of a healed incision from a laparoscopic cholecystectomy, performed 18 months earlier, for treatment of symptomatic gallstones.

3. Discussion

After discussing this patient's case, it was agreed upon that the umbilical metastasis was a result of the prior cholecystectomy and that her cervical cancer seeded in this site. The first report, to our knowledge, of port-site metastasis following a laparoscopic surgery describes a patient with malignant ascites who developed port-site metastasis 2 weeks after undergoing surgery [7]; the report led to concern about whether laparoscopic surgery was appropriate for oncologic surgeries. It has subsequently been found that port-site metastases are most commonly seen in laparoscopic surgeries for treatment of kidney, bladder, and colon cancers [8]. Zivanovic et al. in 2008 reported that of 1694 patients undergoing laparoscopic procedures for the treatment of intraabdominal malignancies, 20 patients (1.18%) experienced trochar-related subcutaneous tumor implants [9].

Cervical cancer port-site metastasis is very rare. In 1994, Childers et al. reported their institution's abdominal-wall tumor implantation rate after laparoscopic surgeries for gynecologic malignancies, and found that no patients with cervical cancer developed a tumor implantation in the incision site [10]. A 2004 retrospective analysis of subcutaneous tumor implantation following laparoscopic surgeries found that there were no isolated cases of a cervical cancer trochar-related metastasis, and that all of the subcutaneous tumor implantations (13 patients, 0.97% of all patients) occurred with either carcinomatosis, synchronous metastases to other sites, or in the setting of a previous laparoscopic surgery in the presence of malignancy in the abdomen and pelvis [11]. In a 2005, retrospective analysis Chen et al. found that 1 patient (0.3%) of 295 who underwent laparoscopic radical hysterectomy and lymphadenectomy for the treatment of cervical cancer experienced a port-site metastasis [12].

Several possible mechanisms of the development of port-site metastasis have been previously described for cases in which metastasis occurs following surgery for treatment of the primary disease. Kohlberger et al. described the "chimney effect" as a possible explanation, in which case tumor cells that have been dislodged from the cervix during surgery can rise to the port site due to pneumoperitoneum [13]. Kadar postulated that a cause of port-site metastasis is that tissue early in the state of healing is more conducive to tumor growth and development than fully healed and normal tissue, and that direct inoculation of the wound is necessary to sustained tumor growth [14]. Gregor et al. suggested that port-site metastasis was related to port-site incision irritation and spillage of tumor cells [16].

In a retrospective review of 24 patients with metastatic primary and recurrent gynecologic cancers, Kadar previously reported that 2 women (8%) with metastatic cervical cancer developed a port-site metastasis [14]. The 2 women who experienced the port-site metastasis did not have their trochar sites treated with

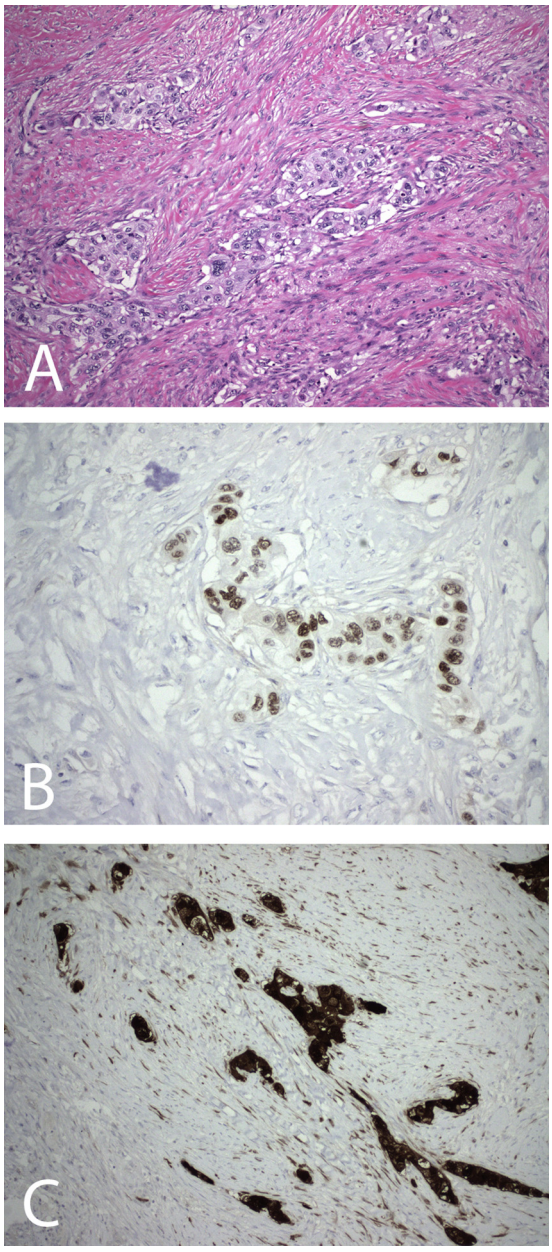

Fig. 4. (A) A representative histological section of the umbilical mass shows nests of carcinoma cells embedded in a dense fibrous stroma. These cells are morphologically identical to the cells of the primary cervical tumor (Fig. 2A). (B) Immunohistochemical studies using p63 demonstrate that the malignant cells are squamous in origin. (C) A positive p16ink4a immunostain further reveals that the malignant cells originate from the cervical primary.

postoperative radiation or chemotherapy, a factor that was found to be statistically significant in reducing the rate of port-site metastases. A 2013 review article by Freitas and Barbosa describes technical surgical methods that could reduce the rate of port-site metastases, including minimal tumor manipulation, resection of the tumor with adequate margins, peritoneal lavage with heparin to avoid adhesions of free cells, use of protective bags for tissue retrieval, avoidance of CO_2 leaks or sudden desufflation, exsufflation of the peritoneum prior to removal of ports, irrigation of ports with heparin solution, and administration of systemic or intraperitoneal methotrexate [15].

4. Conclusion

The case of our patient is quite unusual given that the port-site metastasis occurred at the healed incision of an unrelated surgery (laparoscopic cholecystectomy) conducted 18 months before the diagnosis of cervical cancer. The published literature on cervical port-site metastasis, to the best of our knowledge, solely describes cases of port-site metastasis following surgery for treatment of a newly diagnosed cervical cancer. In our case, the patient did not undergo any other operations in the interval between the cholecystectomy and the removal of the incisional metastatic lesion. If the above-mentioned theories about port-site metastases are to be applied to our case, it must be assumed that microscopic disease became implanted in the umbilical incision site at the time of the cholecystectomy, which would make this case an extraordinarily rare occurrence.

Conflict of interest

None.

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Ethical approval

None.

Consent

None.

Author contributions

Shivam Kharod collected and interpreted data and drafted the manuscript. He was the primary author.

Dr. Anamaria Yeung interpreted data and contributed to writing the manuscript. She was the primary physician directing the contents and treatment plans for this patient.

Dr. Kristianna Fredenburg interpreted pathology data and contributed to writing the manuscript. She prepared the pathology photographs and appropriate descriptions.

Dr. Julie Greenwalt interpreted data and contributed to writing the manuscript. She collected the clinical information, and processed the information adequately for the paper.

Guarantors

Shivam Kharod, Anamaria Yeung, Kristianna Fredenburg, and Julie Greenwalt.

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