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Dorcas C Morgan, Natalie Berger, Konstantin Zakashansky

ABSTRACT

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Case Report: A 66-year-old woman with a known history of colon carcinoma presented with increasing carcinoembryonic antigen (CEA) levels six months after resection of primary adenocarcinoma of the transverse colon. Two inconclusive PET/CT scans were performed over two years in an effort to identify disease. Carcinoembryonic antigen continued to rise. Two years after the initial rise in CEA, a hypermetabolic area in the uterus, initially thought to be a uterine leiomyoma, was deemed suspicious on PET/CT scan. Total laparoscopic hysterectomy and bilateral salpingo-oophorectomy confirmed the diagnosis of metastatic adenocarcinoma of colonic origin in the uterine serosa, myometrium and endometrium.

Conclusion: Approximately, 200 cases of extragenital primaries with metastasis to the female genital tract have been described. Of those, breast is the most commonly seen followed by colon cancer. While colon cancer is known to metastasize to the ovaries, metastatic spread to the uterus is possible as well [1]. Therefore, all postmenopausal women undergoing surgery for colorectal cancer should be counseled regarding possible metastatic disease in the ovaries and/or uterus and should consider removal of these organs at the time of the initial surgery for staging of disease.

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CASE REPORT

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Keywords: Colon cancer, Postmenopausal women, Uterus, Uterine leiomyoma

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INTRODUCTION

Colon cancer is the third most common cancer and the third leading cause of cancer death in women. It is treated surgically. Prophylactic oophorectomy is a consideration when women are undergoing surgery for the treatment of colon cancer and are through with childbearing. This addresses concerns of possible metastasis of colon cancer to the ovary. It is believed that the ovaries appear to be a fertile bed for metastases and a sanctuary site for chemotherapy. Our report indicates that the uterine body may harbor metastases as well without ovarian involvement. The presence of uterine leiomyoma may present additional difficulty in making timely diagnosis of recurrence. Uterine leiomyoma is the most common tumor of female reproductive tract. They may have hypermetabolic activity on positron emission

tomography–computed tomography (PET-CT) scan. This activity may vary with reproductive age. Metastatic disease from the colon to the uterus is rare [1]. Therefore, the removal of the uterus, a hysterectomy, is usually not considered when a woman is undergoing surgery for colon cancer. We present a case of recurrent colon cancer in the uterus initially thought to be a uterine leiomyoma on PET-CT scan.

CASE REPORT

A 66-year-old female G2P2002 was diagnosed with colon cancer on routine colonoscopy. She underwent colonic resection for adenocarcinoma of the transverse colon (pT4apNoMx). Surgical pathology showed a moderately differentiated adenocarcinoma, grossly measuring 4.0x3.5 cm, infiltrating through the serosa onto a small portion of adherent omentum. No lymphovascular invasion was seen. Seventeen regional lymph nodes were negative for cancer cells. Resected margins were free of disease. Surgery was followed by adjuvant chemotherapy with xeloda for six months, which the patient tolerated well.

The patient was doing well, however, six months after surgery her carcinoembryonic antigen (CEA) rose from 2.2–3.4 ng/mL. The patient was monitored closely. Eight months after the surgery, CEA continued to be elevated, 3.5 ng/mL, although her examination was unremarkable. A PET-CT scan was performed and showed no evidence of metastatic disease. Ten months after her initial surgery the CEA continued to rise and was 10.7 ng/mL. Another PET-CT scan was performed. Results revealed an area of focal hypermetabolism along the left lateral uterine fundus versus the left adnexa, maximum SUV 8.3. Further evaluation with pelvic magnetic resonance imaging (MRI) scan suggested a left intramural fundal uterine leiomyoma with submucosal extension measuring 2.2x2.2x2.3 cm. This corresponded to the area of concern on the prior PET-CT scan.

Tumor markers continued to be followed and CEA levels continued to rise. A PET-CT scan was repeated 32 months after the original surgery, and reported that the hypermetabolism was again present along the left lateral uterine fundus; however it was unusually high for a myoma with an SUV of 8.8. Another pelvic ultrasound was recommended. The CEA level at that time was 27.1 ng/mL. CEA levels rose to 46.1 ng/mL and another PET/CT scan, 3 years and 1 month after the original surgery was performed. It again demonstrated continued increase in metabolic activity in the left uterine fundus. Another hypermetabolic area was seen posterior to the uterus, (Figure 1) which likely represented a lymph node. The patient was referred to gynecologic oncology. She underwent a laparoscopic total hysterectomy and bilateral salpingo-oophorectomy. The left lower uterine segment was described as having an exophytic lesion suggestive of cancer grossly extending into the uterine

Figure 1: PET-CT scan showing an area of hypermetabolic activity in the uterus.

myometrium. The lesion measured 2.8 cm x 2.6 cm. The tumor was located in the lower anterior uterine wall, involving the serosal margin. It penetrated the uterine serosa, went through the myometrium and involved the endometrium. No lymphovascular invasion was seen. The cervix, both ovaries and fallopian tubes were free of carcinoma. Immunohistochemical stains revealed tumor cells positive for AE1/3, CK20, CDX2, and TTF1 (focal and weak) and negative for CK7, GCDPF-15, HepPar1, Napsin A, PAX8, synaptophysin, vimentin, ER and PR. The Ki-67 labeling index was about 40%. These results were consistent with the patient's known colon carcinoma.

DISCUSSION

Colorectal cancer is the third most common cancer affecting women and the third most common cause of cancer death in women. Colon cancer is known to metastasize to the lymph nodes, lungs, liver, and peritoneum. Within the female genital tract it is known to metastasize to the ovaries, however, uterine metastases

are rare [1]. Colon cancer is usually treated surgically and depending on the stage, adjuvant chemotherapy may be offered. Close follow-up within the first two years of resection is imperative to identify recurrences within a timely manner. In 1964 Gold and Freedman [2] reported their identification a tumor specific antigen for human colonic carcinoma, CEA. Since then it has been widely used to monitor response to treatment interventions as well as recurrence of disease. Increasing CEA require additional test be performed to detect recurrences, these include computed tomography (CT) scan or magnetic resonance imaging (MRI) scan of the abdomen and chest, MRI and possible positron emission tomography (PET) scan.

The PET-CT scans with FDG (^{18}F -fluorodeoxyglucose) are commonly used at the initial disease staging as well as monitoring for recurrent disease. The FDG usually gives off higher signal (SUV) in the areas where malignant cells are present. However, benign tissues with high cell turnover rate are known to have higher FDG uptake rates. In the case of this patient, it was believed that her uterine leiomyoma was the likely source of the increased uptake. The literature varies in its reporting of FDG activity in leiomyomas. Recent studies suggest FDG uptake in uterine leiomyomas may be influenced by estrogen. Kitajima et al. [3] reported mean values of the maximum and average SUVs for a total of 61 leiomyomas were 2.34 ± 0.75 and 1.74 ± 0.5 , respectively. They reported a negative correlation between maximum and average SUVs and age. In a postmenopausal woman, therefore, the FDG uptake should be low. In this patient it was much higher than reported for any age woman with leiomyomas. Nishizawa et al. [4] also reported FDG uptake in uterine leiomyomas in pre- and postmenopausal women. The uptake was reported in 10.4 % of premenopausal women and only 1.4% of postmenopausal women. The uptake was reported to vary with the menstrual cycle and usually disappeared with menopause. SUV's varied from 3.5 to 16. Lerman et al. [5] conducted a retrospective study investigating the FDG uptake in uterine leiomyomas in women with non-gynecologic malignancies who underwent PET-CT scans. They were able to categorize women based on menstrual cycle and menopause status as well as women with known exposure to selective estrogen receptor modulators (SERMs). They found that the mean FDG uptake was significantly higher in premenopausal women when compared to postmenopausal, 1.47 ± 0.32 SUV compared to 1.29 ± 0.41 SUV. Women with a history of breast cancer and SERM were found to have significantly lower FDG uptake in their uterine leiomyomas compared to untreated women. The SUV's reported in our patient varied from 8.3 to 8.8 were therefore higher than reported in any of the studies in postmenopausal women.

Women diagnosed with colorectal cancer have been found to have metastatic disease to the ovaries 3–14% [6]. The exact mechanism is not clear. Many mechanisms have been proposed including hematogenous and

lymphatic spread to direct extension [7]. Because of this concern, there has been support, albeit controversial that women who undergo surgical intervention for treatment of colorectal cancer be counseled to have removal of both ovaries at the time of the initial surgery even if there no evidence of disease on imaging studies [8]. In our case, we present a rare finding of colorectal cancer metastasizing to the uterus. Extragenital primary cancers metastasizing to the uterus was reported in a small case series [1]. There were 11 cases identified at autopsy or surgery. They had documented metastasis from colon to uterus and were more likely to involve the myometrium and spare the endometrium. Our patient had involvement of serosa, myometrium and endometrium. And while there was microscopic and gross evidence of metastasis in our patient, she did not have a history of postmenopausal bleeding and therefore did not have a clinical indication for evaluating her endometrium. At the time of the hysterectomy, her ovaries appeared free of disease and were not found to have histological evidence of metastasis.

CONCLUSION

Our case demonstrates a rare finding of a isolated colorectal cancer metastasis to the uterus in a patient with a known history of uterine leiomyomas. Caution is required in interpreting PET-CT scan results in patients with uterine fibroids. A consideration should be given to performing prophylactic hysterectomy at the time of prophylactic oophorectomy in patients with advanced colon cancer.

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Author Contributions

Dorcas C Morgan – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Natalie Berger – Acquisition of data, Analysis and interpretation of data, Drafting the article, Final approval of the version to be published

Konstantin Zakashansky – Substantial contributions to conception and design, Revising it critically for important intellectual content, Final approval of the version to be published

Guarantor

The corresponding author is the guarantor of submission.

Conflict of Interest

Authors declare no conflict of interest.

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