Journal of Clinical and Investigative Surgery

https://doi.org/10.25083/2559-5555
https://proscholar.org/jcis/
ISSN: 2559-5555

Malignant transformation of endometriosis on vaginal cuff after hysterectomy: a case report

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ABSTRACT

Objective. Endometriotic tissue implants rarely transform to malignant tissue, especially in a patient with a hysterectomy and bilaterally salpingo-oophorectomy. However, several cases with cancer arising from endometriosis after hysterectomy were reported in the literature. Hormone replacement therapy only with estrogen is a crucial risk factor for malignant transformation of persistent endometriotic tissue. *Case Report*. The present case demonstrates an endometrioid adenocarcinoma arising from persistent endometriosis tissue in a patient who was performed hysterectomy with bilateral salpingectomy 3 years ago. The histopathologic specimens of the previous surgery did not include any malignant tissue. After 3 years, she applied to the hospital with abnormal vaginal bleeding, and her histopathologic examination result found an ulcerated mass at the upper one-third of the vagina that is compatible with endometrioid adenocarcinoma. *Conclusion*. It is crucial to keep in mind the endometriosis history of the patient, to be able to diagnose cancer arising from endometriosis while evaluating the patient with a hysterectomy.

Category: Case Presentation

Received: June 22, 2021
Accepted: August 14, 2021
Published: November 15, 2021

Keywords:

malignant transformation, endometriosis, vaginal cuff, hysterectomy, extragonadal focus

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Introduction

Endometriosis is a hormone-dependent benign disease with a prevalence between 5% to 15% among females worldwide. There are several hypotheses that explain the becoming of endometriosis: i) retrograde menstruation and implantation; ii) coelomic metaplasia; iii) venous or lymphatic spread. All three features belong to both benign and malign processes. A long history of endometriosis was found associated with an increased risk of ovarian cancer [1]. Malignant transformation risk of endometriosis is very low with an incidence of 0.7% [2]. Sampson's criteria are used to determine the malignant transformation in endometriosis: i) endometriotic tissue should be seen near to the tumor; ii) there should not be any other primary site of the tumor; iii) histopathological examination should be similar to the endometrial origin. Scott added one more criterion as demonstrating the transformation of endometriosis into malignant tissue, which will later be called atypical ovarian endometriosis [3].

The present study presents a case with malignancy that arose from endometriotic tissue at the upper vagina after hysterectomy due to uterine fibroid. Interestingly, the case had no history of endometriosis before. Written informed consent of the patient was obtained.

Case Presentation

A 48-year-old female patient with abnormal vaginal bleeding applied to the Department of Obstetrics and Gynecology of Dokuz Eylul University Hospital on 23rd December of 2020 outpatient. The abnormal vaginal bleeding symptom has started four days ago and got increased over time. She had two deliveries via cesarean section (C/S) and she had hypertension as comorbidity. She had a surgery history of laparotomic hysterectomy with bilateral salpingectomy due to medical therapy-resistant abnormal vaginal bleeding caused by uterine fibroid, three years ago. No malignant tissue was detected in the pathologic examination. There were no symptoms till this application. She had no positive family cancer history.

To cite this article: Orkun Ilgen, Sefa Kurt, Deniz Gokcay, Emine Cagnur Ulukus. Malignant transformation of endometriosis on vaginal cuff after hysterectomy: a case report. *J Clin Invest Surg*. 2021;6(2):161-165. doi: 10.25083/2559.5555/6.2.13

Her vital signs were stable and she was conscious on her physical examination. Cardio-respiratory and abdominal examination was detected as normal. On vaginal examination, approximately 3x2 cm diameter, an ulcerated mass was visualized at the upper one-third of the vagina (Figure 1). On ultrasonography (USG), 3x2x2 cm diameter mass was detected at the same localization and bilaterally ovaries seemed normal and no other pelvic pathology was determined. A biopsy was taken from the ulcerated lesion. The patient was discharged on the same day. However, pathology result was compatible with endometrioid adenocarcinoma. Laboratory findings including complete blood count (CBC), coagulation profile, liver, renal function tests, and electrolyte levels were found in normal ranges. Although the cancer antigen 125 (CA-125) level was determined in normal ranges with the level of 20.3 IU/mL, the cancer antigen 19-9 (CA-19-9) level was found increased with the level of 78.80 IU/mL. The patient was scanned by positron emission tomography-computed tomography (PET-CT) in terms of whether there was any other suspicious lesion in the whole body. No other suspicious lesion was detected in PET-CT scanning except an increased F-18 FDG (SUVmax=7.5) uptake in a 3x2x2 cm diameter mass at the level of vaginal cuff (Figure 2). FDG uptake of bilateral ovaries was detected in physiologic ranges.

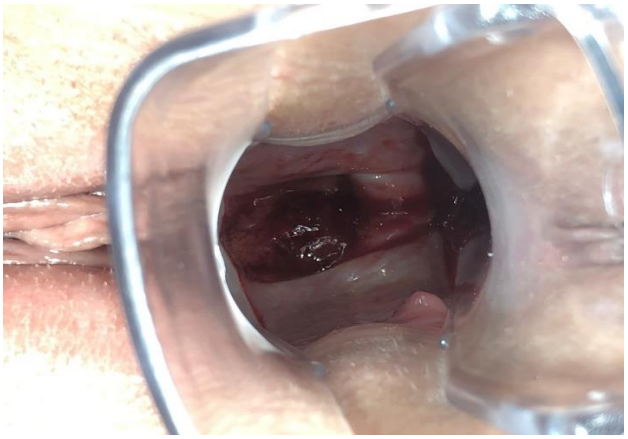

Figure 1. Ulcerated tumoral mass at the upper one-third of the vagina in gynecological examination

Laparotomy was performed on the patient. Bilaterally ovaries were considered normal. First, a pre-operative peritoneal washing fluid sample was collected. After that, bilaterally ovaries were removed followed by infracolic omentectomy. Subsequently, the bladder and rectum were separated from vaginal walls with sharp and blunt dissections. Afterwards, the upper one-third of the vagina with tumor and the parametria were removed. There was no perioperative or postoperative complication. The patient was discharged from the hospital with well-being on the post-operative 3rd day. Well-differentiated endometrioid adenocarcinoma was determined at the final pathologic specimen including atypical cells forming solid glands.

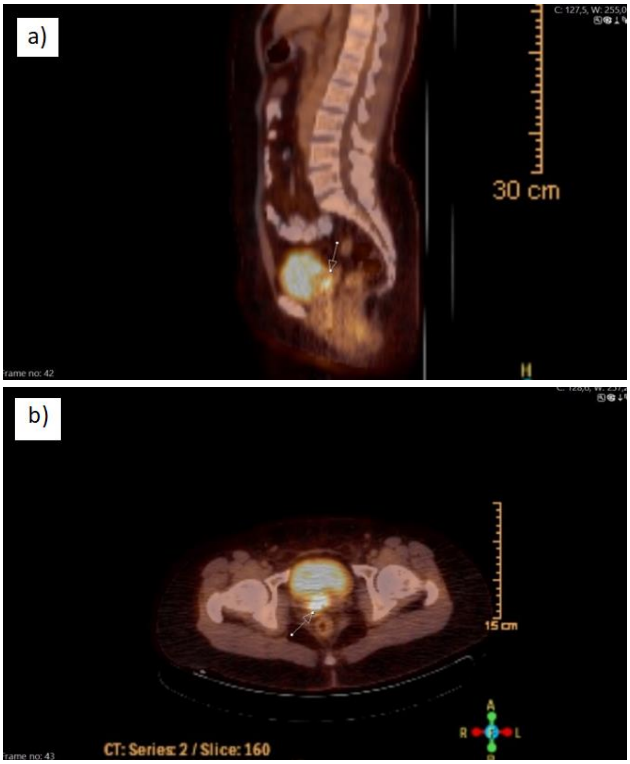

Figure 2 (a, b). Tumoral mass at the upper vagina in PET-CT

A pleomorphic nucleus and increased nucleus to cytoplasm ratio were observed in the histopathologic examination. Moreover, multiple endometriosis focuses were observed in neighbor to tumoral tissue (Figure 3).

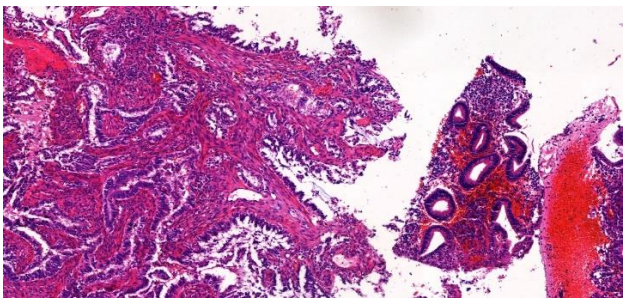

Figure 3. Endometrial tissue fragment containing cytologically benign endometrioid type glands is seen on the right side of the figure. Adenocarcinoma is on the left (H&E, original magnification x10).

This finding also fits in one of Sampson's criteria. Cluster of differentiation 10 (CD10), estrogen receptor (ER), and progesterone receptor (PR) positivity was detected in the specimen by immunochemistry. Besides, paired box gene 8 (PAX8), vimentin positivity and decreased phosphatase and tensin homolog (PTEN) gene expression were determined. On the other hand, p16 immunostaining was negative in the specimen. No malignant tissue was observed in bilaterally ovaries and omentum by histopathologic examination. Endometriosis also was observed in the right ovary. There were no malignant cells in the peritoneal washing fluid.

Radiotherapy and 6 cycles of carboplatin and paclitaxel chemotherapy every 3 weeks were planned to perform on the patient. Her follow-up in the gynecologic oncology clinic was scheduled.

Discussion

Functional endometrial tissue outside the uterine cavity is called endometriosis. It is a very common disorder among females with an incidence of 7% [4]. The disease frequently is seen in pelvic organs including ovaries, the pouch of Douglas, broad ligament, etc. Ovaries are the most frequently involved organ in endometriosis. Besides, endometriosis was determined in any other organs in the abdomen even in the thorax [5]. Transformation of endometriosis into malignant tissue is rare. Atypical cells in endometriotic tissue without a neoplasm are detected in 2% of the patients. Moreover, neoplasm risk arising from endometriotic tissue is approximately 0.7% [6]. Older age, increased duration of endometriosis, longer exposure to the abnormal inflammatory process and genetic predisposition are the defined risk factors for malignant transformation of endometriosis. Endometrioid and clear cell adenocarcinoma is the most common type of cancers that are determined arose from the endometriotic focus. According to a study conducted by Pearce et al., threefold increased risk for clear cell carcinoma and twofold increased risk for endometrioid adenocarcinoma were found [7]. Moreover, in another study, it was found that ovarian cancer patients with endometriosis have a better prognosis than those without endometriosis [8]. In the present case, endometrioid adenocarcinoma was seen. Also, breast cancer and non-Hodgkin's lymphoma incidence was found increased in endometriosis patients according to several studies [9-11].

Ovary is the most common localization for developing cancer in endometriosis patients with an incidence of 75%. However, extragonadal malignancy in endometriosis was observed at other areas including the pouch of Douglas, colorectal region, bladder, and vagina [12]. In the present report, upper one-third of the vagina was involved by cancer cells arising from endometriosis. Hormone replacement therapy (HRT) with unopposed estrogen in postmenopausal patients was found associated with the increased risk of cancer development in endometriosis patients [13]. On the other hand, HRT with the estrogen-progesterone combination is the preferred regime that was also recommended by the European Menopause and Andropause Society (EMAS) in postmenopausal women with a history of endometriosis [14]. However, the present case did not use HRT as ovaries were protected at the previous surgery.

There were several cases in the literature regarding endometriosis-associated malignancy after hysterectomy and bilaterally salpingo-oophorectomy [15-17]. Management strategies for this sort of rare cases are controversial. Endometriosis-associated ovarian cancers are frequently low-grade, therefore, using chemotherapy in these cases is controversial. However, a study conducted by Davis et al. showed that the efficacy of chemotherapy is similar between serous papillary ovarian cancer and ovarian cancer arising from endometriosis [18]. R_0 resection followed by adjuvant chemotherapy is the recommended method for endometriosis-associated cancers as in usual standard ovarian cancer treatment. In a previous study, certain patients with disease confined to the pelvis was treated with radiotherapy ± progestin therapy after the surgery and this method was found effective to control the disease with the 77% 5-year survival rates [19]. In the present case, both chemotherapy and radiotherapy were planned to perform on the patient in accordance with the literature.

Highlights

- ✓ Endometrioid adenocarcinoma arising from endometriosis in a patient with a history of performed hysterectomy is a rare tumor worldwide.
- ✓ Prognosis and treatment protocols are not definite due to the lack of case numbers.

Conclusions

Cancers arising from endometriosis are rare, however, it can be even seen at extragonadal places in patients who were performed hysterectomy under benign conditions. It is crucial to keep in mind the endometriosis history of the patient to diagnose cancer arising from endometriosis while evaluating the patient with a hysterectomy who applies to a gynecology clinic with abnormal vaginal bleeding and pelvic tumoral mass.

Accordingly, endometrioid adenocarcinoma arising from endometriosis can be diagnosed by suspicion and looking from a broad perspective in a patient with a history of prior hysterectomy and can be well treated with a multidisciplinary team including gynecologic oncologists and pathologists.

Conflict of interest disclosure

There are no known conflicts of interest in the publication of this article. The manuscript was read and approved by all authors.

Compliance with ethical standards

This report followed guidelines to be HIPAA compliant and permission was obtained from the patient to publish identifiable photographs. The study adhered to the tenets of the Declaration of Helsinki. Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Author Contributions Statement

OI: manuscript writing, data collection;
SK: review of the manuscript, data collection;
DG: manuscript writing;
ECU: review of the manuscript, supervision.

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