

Vaginal Endometrioid Adenocarcinoma Arising from Endometriosis after Total Abdominal Hysterectomy and Bilateral Salpingo-Oophorectomy

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Abstract

Primary carcinoma of the vagina accounts for 1% of gynecologic malignancies. Adenocarcinoma is the second most common primary cancer in the vagina. Although less common than squamous cell carcinoma, it represents 15% of all primary vaginal malignancies. The most common manifestation of this malignancy is postmenopausal bleeding as in the current case. Specific criteria in establishing endometriosis-related malignancy as presented by Sampson include the presence of benign endometrial and malignant tissue at the same site, the presence of endometrial stroma surrounding glands, and the exclusion of metastasis from another primary site. This is a case of a 63-year-old gravida 1 para 1 (1001), who presented with postmenopausal bleeding with history of previous total abdominal hysterectomy and bilateral salpingo-oophorectomy two decades past. A three-centimeter vaginal mass was appreciated on internal examination. Vaginal biopsy revealed vaginal endometrioid adenocarcinoma. No metastasis noted. The patient underwent surgery where the specimen revealed vaginal endometrioid adenocarcinoma.

Keywords: Adenocarcinoma, Endometriosis, Hysterectomy, Postmenopausal Bleeding, Vaginal Cancer.

Received: October 01, 2025;

Accepted: October 07, 2025;

Published: October 15, 2025

Introduction

Primary endometrioid adenocarcinoma rarely occurs in the vagina and accounts for 8 to 10% of cases [1]. Vaginal malignancy that is associated with endometriosis is exceedingly rare [2]. The frequency of malignant transformation of endometriosis is unknown. Ages of patients mostly affected are ranging from 45 to 81 years old. The most frequent manifestation was vaginal bleeding. Hyperestrogenism is a significant risk factor for the development of cancer from endometriosis [3].

Herein is a report of a case of primary vaginal endometrioid adenocarcinoma associated with endometriosis who underwent total abdominal hysterectomy and bilateral salpingo-oophorectomy for endometriosis two decades earlier.

Case Report

This is a case of a 63-year-old gravida 1 para 1 (1001), with no known comorbidities and with history of previous total abdominal hysterectomy and bilateral salpingo-oophorectomy (TAHBSO) for endometriosis

20 years ago. The patient is a non-smoker and a non-alcohol beverage drinker, with a family history of pancreatic cancer.

History started one month prior when she experienced sudden onset postmenopausal bleeding described as lightly staining her underwear. There were no other accompanying symptoms such as pelvic heaviness, bowel and bladder changes, unintentional weight loss, or anorexia. She sought consult and a three-centimeter vaginal mass was appreciated on pelvic examination. Papanicolaou smear was negative while vaginal stump biopsy revealed endometrioid adenocarcinoma, FIGO grade 2. Immunohistochemical stains showed focal positive results for p40 and CEA, positive in stromal component for CD10, and negative for ER and SMA. With these, the patient was referred for subspecialty consultation. Patient was examined and a whole-body Positron Emission Tomography – Computed Tomography (PET-CT) with diagnostic CT was requested which revealed hypermetabolic lesion in the left aspect of the vaginal stump, with no hypermetabolic nodes

Citation: Roxanne Gillea G Tan, and Leo Francis N Aquilizan (2025) Vaginal Endometrioid Adenocarcinoma Arising from Endometriosis after Total Abdominal Hysterectomy and Bilateral Salpingo-Oophorectomy. *J Gyne Womens Heal Care* 1: 1-4.

in the pelvis and abdomen and no hyperbolic distant metastasis (Figure 1); hence, the patient was advised surgery.

The patient had a normal ejection fraction of 80% on 2D Echocardiogram, normal electrocardiogram, normal complete blood count and normal cancer antigen (CA) 125 (Table 1). Once cleared for operation, peritoneal fluid sampling, excision of vaginal mass, vaginectomy, bilateral lymph node dissection, and omentectomy under combined regional – general anesthesia was performed. Intraoperative findings revealed a palpated vaginal mass measuring approximately four centimeters seemingly not adherent to the vaginal walls on internal examination. The vaginal mass measured five centimeters in its widest diameter with no gross infiltration into the bladder, rectum, or side walls. The abdominal cavity was also evaluated for evidence of metastasis where in the liver, diaphragm, and spleen were noted to be smooth. There was no noted carcinomatosis. Collected specimens were sent for histopathology. Vaginal tumor revealed poorly differentiated endometrioid adenocarcinoma, FIGO grade 3, with associated endometriosis and lymphovascular invasion identified on the vagina (Table 2) The patient tolerated the procedure well with no intraoperative complications and was discharged stable.

Histopathology slides showed that an area of the cervix revealed solid sheets and nests of neoplastic cells with presence of a gland which resembles an endometriotic gland which denotes an endometriosis at the upper portion of the tumor (Figure 2-B).

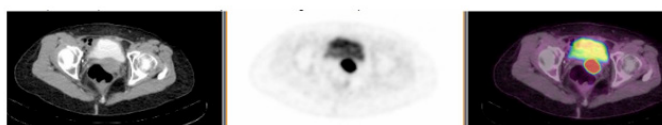


Figure 1: PET CT SCAN. Uterus and ovaries are surgically absent. No discrete enhancing pelvic mass lesion seen in the CT scan. A FDG-avid lesion (SUV 9.1) is seen in the left aspect of the vaginal stump. No evidence of ascites or pneumoperitoneum. No enlarged lymph nodes (abdominal-pelvic-inguinal). No FDG-avid pelvic and abdominal nodes seen.

Table 1: Laboratory Tests

Test	Actual Result	Normal Value
Complete Blood Count		
Hemoglobin	11.1	11.6 – 15.5
Hematocrit	33.0	36.0 – 47.0
Red Blood Cell	3.63	4.20 – 5.40
White Blood Cell	8400	4800 – 10800
Differential Count		
Neutrophils	86	40 – 74
Lymphocytes	3	19 – 48
Monocytes	2	3 – 9
Stabs	9	2 – 6
Platelets	183000	150000 – 400000
MCV	91	82 – 98
MCH	31	28 – 33

MCHC	34	32 – 38
RDW	12.8	11 – 14
CA 125	7.30	0 - 35

Table 2: Surgical Histopathology

Specimen	Diagnosis
A. Cul De Sac Peritoneum	Fibrocollagenous tissue with chronic inflammation Negative for tumor
B. Vaginal Tumor	High grade carcinoma Poorly differentiated endometrioid adenocarcinoma (FIGO grade III)
C. Vagina with Suture on 12 O'clock	High grade carcinoma Poorly differentiated endometrioid adenocarcinoma (FIGO grade III) Lymphovascular invasion identified Surgical margins (Distal margin and base), Negative for tumor Endometriosis
D. Bladder Peritoneum	Positive for tumor along perivesical tissue
E. Left Pelvic Lymph Node	One lymph node with isolated tumor cells within afferent lymphatics Five lymph nodes, negative for tumor
F. Left Pelvic Side Wall	Benign Fibroadipose Tissue Negative for tumor
G. Right Pelvic Side Wall	Benign Fibromuscular Tissue Negative for tumor
H. Right Pelvic Node	Seven lymph nodes, negative for tumor
I. Omentum	Benign Fibroadipose Tissue

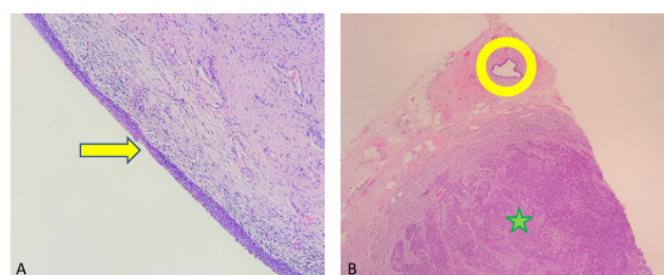


Figure 2: Section of Cervix. A.) The ectocervix is lined by squamous epithelium (yellow arrow); B.) Area of cervix solid sheets and nests of neoplastic cells (green star). Endometrial gland (yellow circle)

Case Discussion

Primary carcinoma of the vagina is rare. It constitutes about one percent of gynecologic cancers [4]. Primary adenocarcinoma of the vagina is uncommon. Even though uncommon, it is the second most common primary cancer of the vagina. It represents only about 14 to 15% of all primary carcinomas of the vagina. Less than 20% of vaginal adenocarcinomas are primary tumors [5]. It accounts for 8 to 10% of cases [1].

Cancer of the Vagina is a very rare malignancy that accounts for a lifetime risk of 0.09% among women. Based on the GLOBOCAN statistics in 2018, vaginal cancer only accounts for 0.1% of all new cancer cases across 185 countries. In the Philippines, there was no record of vaginal cancer in PGH last 2018 based on their archives. In Jose Reyes, there was only one new vaginal cancer case out of the 723 new gynecologic cases noted. On primary adenocarcinoma of the vagina, only one case was reported in our institution since 2017.

Endometriosis is the growth of endometrial-like glandular epithelium and stroma outside the uterus. It is a chronic and benign gynecologic disease. It occurs 10 to 15% in women of reproductive age, 20 to 30% in women with infertility, and 40 to 60% in women with chronic pelvic pain. In the case presented, the patient had history of endometriosis. Vaginal malignancy that are endometriosis-related are exceedingly rare [2]. The frequency of malignant transformation of endometriosis is unknown. Documented cases are rare [6]. Some of the cases reported include studies by Wirtheimer in 1964, Decelle in 1969, Bamford in 1967, Hyman in 1977, Kapp, et al. in 1982, and Granai et al. in 1984. All of the cases were reportedly of women with ages ranging from 35 to 56 years old. They also mostly presented with vaginal bleeding, as with the presented case. Three of the reported cases have prior hysterectomy and oophorectomy. In the presented case, the patient underwent total abdominal hysterectomy with bilateral salpingo-oophorectomy 20 years ago and presented with postmenopausal bleeding. Residual extrauterine endometriosis may undergo malignant transformation even after surgical and hormonal treatment. It is estimated to be about one percent of women with endometriosis may develop malignancy during their lifetime. In the histopathologic findings of the specimen submitted (vagina with suture on 12 o'clock), presence of high-grade carcinoma, poorly differentiated endometrioid adenocarcinoma, and endometriosis were revealed. Frequently, the extragonadal sites involved are the rectovaginal septum, colon, and vagina. The most frequent malignancies arising from endometriosis are endometrioid and clear cell adenocarcinoma. These endometriosis-arising tumors are usually low grade with a favorable prognosis [2].

The pathogenesis of malignant changes in endometriosis is unclear. There are studies which suggest that there are some aspects of endometriosis.

Malignant transformation of endometriosis is an uncommon event. Atypia (intraepithelial neoplasia) in endometriosis is seen in 2% of cases without a neoplasm, and the estimated risk of cancer arising from preexisting endometriosis is approximately 0.7-1.0%.

Considered as one of the main risk factors resulting in malignant transformation of endometriosis is high level circulating estrogen [2]. Hyperestrogenism or unopposed estrogens are significant risk factors for the development of cancer from endometriosis [3].

In a study by Merino, there are many factors predisposing women, older women in particular, to vaginal cancer. Previous hysterectomy for benign disease, such as endometriosis, may be a factor in primary vaginal cancer. There appears to be a strong link existing between endometriosis and primary vaginal cancer. In another study by Bell, et. al., there was a 36% incidence of vaginal carcinoma in 87 women who underwent hysterectomy for benign disease [6,7]. In the case presented, the patient is a 63-year-old, with history of total abdominal hysterectomy with bilateral salpingo-oophorectomy for endometriosis at 43 years old.

Based on a study of a series of 18 cases conducted by Staats, Clement, and Young, ages of patients affected ranged from 45 to 81 years old, which is the case with our 63-year-old patient. The most frequent manifestation was vaginal bleeding and/or postmenopausal bleeding. In 16 out of 18 cases they studied, the patients had undergone hysterectomy for various benign indications, such as endometriosis; while in 14 out of 18 cases, vaginal endometriosis was identified [4]. The present case discussed is an ideal example of a primary case of vaginal endometrioid adenocarcinoma arising from endometriosis after TAHBSO for endometriosis two decades past.

According to the study by Cozzolino, et al., the most common presenting symptom was vaginal bleeding. Other less common symptoms include pelvic pain, vaginal discharge, dyspareunia, and dysmenorrhea. It was also stated that in some cases, patients are initially asymptomatic, or they ignore minor symptoms [2]. In the case presented the patient had sudden onset postmenopausal bleeding described as lightly staining her underwear. There were no other accompanying symptoms such as pelvic heaviness, bowel and bladder changes, unintentional weight loss, or anorexia.

One of the earliest studies on endometrioid adenocarcinoma was conducted at 1925 by John A. Sampson in the Archives of Surgery. Sampson first defined and established specific criteria for diagnosing endometriosis – related malignancy. These included the presence of benign endometrial and malignant tissue at the same site, the presence of endometrial stroma surrounding glands, and the exclusion of metastasis from another primary site [8]. In the histopathologic findings of the patient, it showed that an area of the cervix revealed solid sheets and nests of neoplastic cells with presence of a gland which resembles an endometriotic gland which denotes an endometriosis at the upper portion of the tumor, fulfilling the first and second criteria. A whole-body PET-CT with diagnostic CT was done which showed no hypermetabolic nodes in the pelvis and abdomen and no hyperbolic distant metastasis, fulfilling the third criteria. On the basis of the said criteria, the presented case can be classified as arising from endometriosis. Another study by Scott 1953 suggested that endometriosis should be contiguous with the neoplasm to prove the origin of the tumor from endometriosis [8].

According to Cozzolino, et al., because of the rarity of the malignant transformation of the vaginal endometriotic foci, optimal management of these tumors were not well defined [2]. Surgical management was uniformly employed in majority of the cases, as what was done with our patient. Hormonal therapy of progesterone can also be considered for those with documented residual endometriotic foci to inhibit proliferation.

Conclusion

Primary endometrioid adenocarcinoma of the vagina is the second most common subtype of vaginal adenocarcinoma and accounts to 8 to 10% of cases. In majority of cases, it is seen in association with endometriosis, which is a finding that helps in the exclusion of metastatic disease. Treatment of vaginal carcinoma depends primarily on histology, tumor volume, anatomic location, stage and age of the patient.

Endometriosis is an important medical and social problem. Despite comprehensive research, its origin, natural history, malignant transformation, and laboratory management are not yet clearly investigated.

As clinicians, we have an opportunity to raise awareness and at the same time set up strategies for better prevention, early detection, specific diagnosis and treatment targeting its pathogenesis to better understand the mechanism of endometriosis-associated cancer.

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