

Endometrial Cancer as a Cause of Secondary Postpartum Hemorrhage: A Case Report

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ABSTRACT

Endometrial cancer is the 6th most common cancer in women worldwide. Rarely does occur in the postpartum period. Fifteen cases of endometrial cancer in the postpartum period have been reported before, but the diagnosis of endometrial carcinoma as a cause of secondary postpartum hemorrhage is hardly predicted. A 37-year-old, Para 4, presented two weeks after a cesarean section and had recurrent vaginal bleeding. The patient was treated conservatively. While being observed, vaginal bleeding still occurred with more volume. We decided to perform a total abdominal hysterectomy. Histopathology confirmed a low-grade endometrioid carcinoma of the corpus uteri. Endometrial cancer might cause a secondary postpartum hemorrhage, with the hypothesis that the depth of tumor invasion into the uterine muscle causes a distorted tissue architecture and the formation of new blood vessels that easily disrupt. The most common type of endometrial cancer in a postpartum woman is low grade with a favorable prognosis.

Keywords: Endometrial Cancer, Endometrioid Carcinoma, Postpartum Hemorrhage, Vaginal Bleeding



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Introduction

Endometrial cancer represents the 6th most common malignant disorder in women worldwide, with an estimated number of 382,000 new cases diagnosed with this malignancy in 2018 (1). It typically occurs in peri- or postmenopausal women, and only 5% of women are diagnosed before the age of 40 years; while the diagnosis of endometrial cancer during pregnancy is rare and usually found accidentally due to symptoms of bleeding in early pregnancy or postpartum. In the past 80 years, there have been approximately 30 cases of endometrial cancer coexisting with pregnancy and 15 cases found postpartum (2, 3). In this report, we present a case of endometrial cancer as a cause of secondary postpartum hemorrhage (PPH).

Case Presentation

A 37-year-old woman, para 4, presented with recurrent vaginal bleeding. Her history included two vaginal deliveries and two previous cesarean sections

without any significant complications before or during pregnancy, labor and surgery. Five weeks prior to admission, the patient underwent a second repeat cesarean section. Two weeks after the procedure, she started experiencing vaginal bleeding. She had been admitted to another hospital three times and spent three days in the ICU due to recurrent vaginal bleeding. She received medical treatment for secondary PPH and underwent a transfusion of five Packed Red Cells. The patient had no known history of gynecology or other known illness before the pregnancy, and her Body Mass Index was within the ideal range. There was no history of pap smear examination. There was no history of vaginal bleeding during pregnancy or any placenta abnormalities. There was no family history of malignancy. Upon of admission to our hospital, there were no signs of profuse bleeding. Speculum examination revealed no erosion or mass, and bleeding was not active. Pelvic examination showed normal findings. Trans abdominal ultrasound did not indicate

any significant abnormalities, with an endometrial line measuring 5.34 mm and no signs of retained products of conception. Laboratory tests showed a Hemoglobin level of 7.3 gr/dl, and coagulation test were within normal limits. The patient received a transfusion of two Packed Red Cells and was observed for 48 hours, during which bleeding unexpectedly continued (approximately 500 mL). Profuse bleeding was occurred. After careful consideration and due to the absence of signs or symptoms of malignancy or other gynecology indications from the examinations performed, curettage was not performed. The decision was made to proceed with a total abdominal hysterectomy along with left salpingo-oophorectomy and right salpingectomy, due to secondary PPH. The patient remained in stable condition after surgery and was discharged four days later. Histopathological examination confirmed on microscopic examination of uterine tissue a week after surgery, revealed a tumoral mass consisting of a proliferation of endometrial

glands that forming a tubular, acinar structures and partly arranged back to back between the stroma, lined with atypical columnar epithelial cells, partly pleomorphic with round oval nuclei, enlarged in size, rough chromatin, and some with prominent nucleoli, eosinophilic and granular cytoplasm. The tumoral cells penetrated less than 1/2 of the myometrial layer. With solid non-glandular growth area of <5%. There was evidence of blood vessels proliferation and some of which exhibited atherosclerosis, as well as dilated and congested blood vessels. The tumoral cells infiltrating blood vessels were not found. Lymph vascular space involvement was negative. The conclusion of histopathological examination was a low grade endometrioid carcinoma of the corpus uteri with arteriovenous malformation. The patient was then referred to a tertier oncology gynecologist. A complete staging and further treatment were advised, but the patient declined and opted not to undergo a relaparotomy ([Figure 1](#), [Figure 2](#) and [Figure 3](#)).



Figure 1. Transabdominal ultrasonography shows no significant abnormality at five weeks after the second repeat cesarean section. The length of the uterus was 8.1 cm.

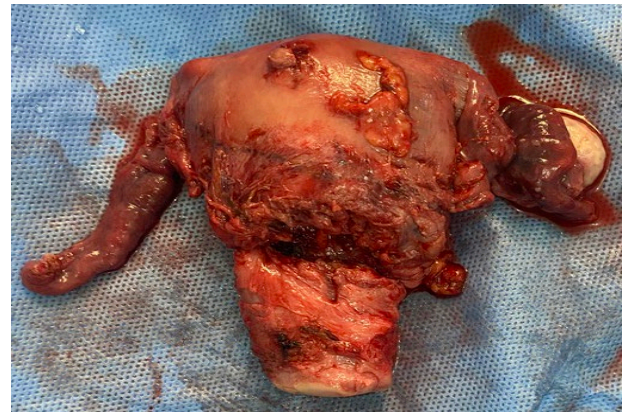
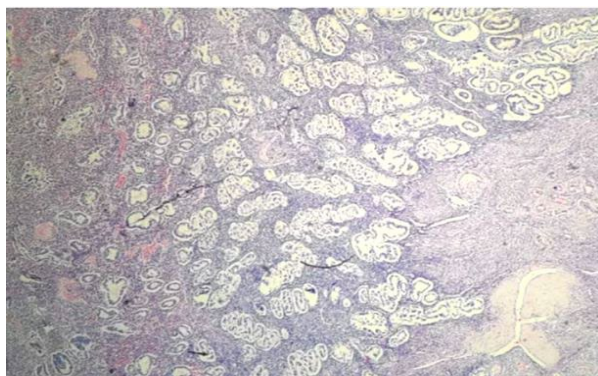
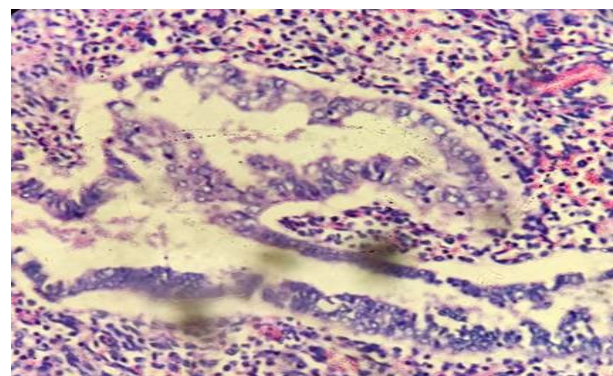


Figure 2. Macroscopic findings in the surgical specimen post total abdominal hysterectomy. Ruptured of the anterior uterus occurred during adhesiolysis due to the adhesion to the bladder.



A



B

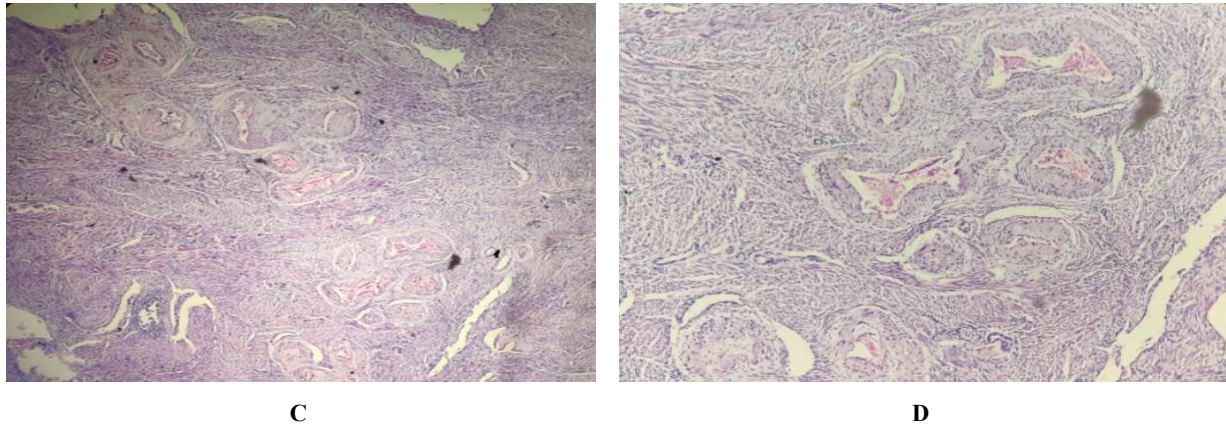


Figure 3. A. Proliferation of the endometrial glands that form a tubular structure, acinar, and partially arranged back to back between the stroma, lined with columnar epithelial cells, tumor cells that penetrate less than 1/2 of the myometrium. (H&E, 40x) B. Atypical, pleomorphic columnar epithelial cells with rounded oval nuclei, enlarged size, coarse chromatin, partially prominent nuclei, eosinophilic and granular cytoplasm. Interstitial bleeding (+). (H&E, 400x) C&D. Blood vessels, and some have arteriosclerosis, dilated and congested blood vessels are also visible. (H&E, 100x)

Discussion

Low grade endometrioid carcinoma of the corpus uteri as a cause of secondary postpartum hemorrhage (PPH) has never been reported before. However, there was a case of 28-year-old patient who presented with secondary PPH and was diagnosed with endometrial stromal sarcoma (4). Also there was a case of 20-year-old primiparous female with a history of vaginal delivery 6 months before her referral with a complaint of menometrorrhagia. On hysteroscopy, a 5 cm mass was found on the anterior wall of the uterus, which was resected, and pathology report showed low-grade endometrial stromal sarcoma (5). In our case, the etiology of secondary PPH has been excluded, including uterine atony, endometritis and retained products of conception (6, 7). It is unusual for endometrial cancer to develop during reproductive age and pregnancy, the development of endometrial cancer due to augmented progesterone secretion and a decreased oestrogenic state should not happen, as it is usually an oestrogen-dependent cancer that occurs in postmenopausal women (1, 8). Pregnancy itself can help prevent the progression of a potential hormone-sensitive disease (9). In many reported cases, spontaneous abortion occurs in pregnancies with endometrial cancer (10). In our case, the patient did not have any complaints until two weeks after repeat cesarean section when she experiences profuse vaginal bleeding.

In one literature review, 14 cases of endometrial cancer in the postpartum period revealed that the majority of patients did not have any identified risk factors, with median age was 32 years, and the most common presenting complaint was abnormal vaginal bleeding in the postpartum period (2).

Endometrial carcinoma is characterized by increased microvessel density compared to the adjacent uninvolved endometrium. This is associated with strong expression of vascular endothelial-growth-

factor (VEGF), which plays a role in initiating physiological and pathological angiogenesis, lymphangiogenesis, and vasculogenesis. When tumor growth is rapid and there is high interstitial pressure, along with larger distances between cancer cells and capillaries, hypoxia occurs. Hypoxia then triggers angiogenesis, leading to the formation of new vasculature in and around the tumor. This new vasculature provides nutrients and oxygen to the tumor cells, allowing for continuous growth and proliferation (11). Doldi, Bassan, investigated the expression of vascular endothelial growth factor transcript in human endometrial carcinoma. Messenger RNA-encoding VEGF was detected in all tissues studied and was more abundant in endometrial carcinoma (12). Those data suggest that VEGF might promote tumoral angiogenesis and stromal generation, acting as endometrial cell mitogen. Guidi et al, also explained all specimens of endometrial carcinoma showed strong, focal VEGF mRNA expression (13). Histologically, the origin of bleeding can be traced to multiple foci of necrosis of malignant tissue, often associated with chronic endometritis of the supportive stroma. Excessive epithelial growth, accompanied by a reduction in peripheral perfusion, can lead to hypoxia. Endothelial integrity might be disturbed and induces vascular breakdown and bleeding. Peripheral tissue necrosis due to intracavitary friction of the malignant mass, neovascular fragility and proteolytic enzyme-related cell destruction of inflammatory cell origin may also contribute to intermittent bleeding in cases of endometrial cancer (14). In our case, the depth of endometrial cancer may explain the cause of recurrent vaginal bleeding and secondary PPH.

There are two classification of grading that has been used for endometrial cancer, FIGO 3-grade assessment of the glandular component and binary histological grading of endometrial carcinoma (Low grade and high

grade). Low grade refers to endometrioid carcinomas with less than 50% solid component and absence of marked nuclear atypia, while high grade refers to those with greater than 50% solid component and/or marked nuclear atypia (15). This recent binary grading is chosen as a preferable prognostic factor, as grade one and two tumors show similar prognosis, and a binary grading system combining these two grades could be simpler. Also, removing grade two from the current grading system may improve risk stratification and help eliminate confusion regarding adjuvant therapy (16). Vaccarello et al, Shiomi et al summarized 52 cases of pregnancies with endometrial cancer, of which 48 cases were found to be grade one and grade two. This indicates that endometrial cancer discovered during pregnancy or the postpartum period is mostly low-grade cancer and has favorable prognoses (3, 17). In a literature review of 14 cases endometrial cancer associated with pregnancy, eleven patients with low grade disease and FIGO stage one in twelve of the cases. They were treated with primary surgery and showed no evidence of disease recurrence over 1-6 years follow up period (2). The surgical treatment for endometrial cancer is surgical staging, which includes total hysterectomy, bilateral salpingo-oophorectomy, and pelvic and para aorta lymphadenectomy. The extent of surgery depends on clinical stage, histology type and differentiation. Adjuvant therapy (such as radiotherapy, chemotherapy, hormonal medicine) after surgery also depends on clinical stage, histology type, differentiation and/or other risk factors. The five-year survival rate for low-grade endometrial cancer is between 69% to 90%. The incidence of ovarian metastasis in women with clinical stage I endometrial cancer has been reported by most studies to be approximately 5%. In our case, restaging is necessary

since one ovary is still remain. Unfortunately, two years after diagnosed with endometrial cancer, the patient still refuses to undergo complete surgery for staging and/or follow up, and has no complaints about her current condition.

Conclusion

This is a rare case. A definitive examination for the diagnosis of endometrial cancer as a cause of secondary postpartum hemorrhage (PPH) has not yet been found. If all etiologies of secondary PPH have been excluded and conservative treatment has not succeeded, endometrial cancer might be suspected, and a hystopathology examination must be ruled out. Therefore, reporting more cases in the long run might provide more data and convenience for clinicians to suspect endometrial cancer as one of the causes of secondary PPH.

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Conflict of Interest

Authors have no conflict of interest related to this work.

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