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RESEARCH ARTICLE
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LOW-GRADE ENDOMETRIOID CARCINOMA PRESENTING AS SECONDARY POSTPARTUM HEMORRHAGE: A RARE CASE REPORT

Aiysha Gul[1]*, Gayathri Gururamalingam[2], Jasmin Ghanbari[3], Marseris Kaid Bay[4], Fath Elrahman Elrasheed[5], Henna Patel[6]

[1*]Department of Obstetrics and Gynaecology, Mardan Medical Complex, Mardan, Pakistan, ayeshag0342@gmail.com
[2]Department of Surgery, Bhagwan Mahaveer Jain hospital, Bangalore, India, gayathriguru63@gmail.com
[3]Department of Obstetrics and Gynaecology, Medical University of Varna, Varna, Bulgaria, Ghanbari.jasmin@gmail.com
[4]Department of Obstetrics and Gynaecology, Universidad de Oriente, Ciudad Bolívar, Venezuela, Dramarserisk@gmail.com
[5]Department of Obstetrics and Gynaecology, Najran University, Najran, Saudi Arabia, fathsaed@yahoo.com
[6]Department of Obstetrics and Gynaecology, GMERS Hospital, Vadodara, India, phenna78@gmail.com

***Corresponding Author:** Aiysha Gul
*Email address: ayeshag0342@gmail.com

Abstract
Endometrial cancer is a rare occurrence in reproductive-aged women, particularly in association with pregnancy or the postpartum period. This case report describes a 28-year-old woman who presented with secondary postpartum hemorrhage (PPH) 10 days after a normal vaginal delivery. Despite the absence of gynecological history and initial normal findings on ultrasound, persistent bleeding led to surgical intervention with a total abdominal hysterectomy. Histopathological examination revealed low-grade endometrioid carcinoma of the uterine corpus associated with arteriovenous malformation. This case highlights the unusual presentation of endometrial cancer during reproductive years, its management, and the importance of considering malignancy in cases of unexplained secondary PPH. Although low-grade endometrial cancer generally has a favorable prognosis, follow-up and complete surgical staging are critical for optimal management and long-term outcomes.

Keywords: Low-grade endometrioid carcinoma, Secondary postpartum hemorrhage, Endometrial cancer in pregnancy, Vascular endothelial growth factor, Premenopausal endometrial cancer, Endometrial cancer in younger

Introduction
Endometrial cancer ranks as the fifteenth most frequent cancer globally and is the sixth most common cancer affecting women (1). The incidence of this cancer is higher in high-income nations,

with 11.1 cases per 100,000 women, compared to 3.3 cases per 100,000 in low-income countries (2).

Endometrial cancer predominantly affects postmenopausal women, with 75–80% of cases diagnosed after menopause. The occurrence of this cancer in premenopausal women ranges from 14 to 20%. It is considered rare, accounting for only 5% of cases, in women under the age of 40 (3).

Around 30 cases of endometrial cancer have been documented during pregnancy, and an additional 15 cases have been identified in the postpartum period (2, 3). This report discusses a case involving a 28-year-old woman, where endometrial cancer was identified as the underlying cause of secondary postpartum hemorrhage (PPH) (4).

Case Presentation

A 28-year-old woman, Para 2, presented with recurrent episodes of vaginal bleeding, her medical history included two previous vaginal deliveries without any major complications during pregnancy or labor. Twenty days before admission, she had a normal vaginal delivery. However, ten days post-delivery, she began experiencing heavy vaginal bleeding. She was referred to a tertiary care hospital for further evaluation. Initial management for secondary postpartum hemorrhage (PPH) included the administration of six units of packed red blood cells. She had no prior history of gynecological issues or other known medical conditions before her pregnancy, and her Body Mass Index was within the healthy range. There was no history of Pap smear examinations or vaginal bleeding during pregnancy, nor were there any placenta-related abnormalities. Her family history was negative for malignancy.

Upon admission to our hospital, there was no active bleeding noted. A speculum examination revealed no signs of erosion or mass and pelvic examination findings were normal. A transabdominal ultrasound showed no significant abnormalities, with the endometrial lining measuring 6.1 mm, and no evidence of retained products of conception. Laboratory tests revealed a hemoglobin level of 7.8 gm/dL, with coagulation profiles and thyroid function tests within normal limits. The patient received two additional units of packed red cells and was monitored for 48 hours, during which she experienced further bleeding, approximately 500 mL. Despite the absence of malignancy signs or other gynecological indications, curettage was not performed.

Considering the persistent bleeding and absence of other clinical findings, a total abdominal hysterectomy, along with a left salpingo-oophorectomy and right salpingectomy, was performed to address secondary PPH. The patient's postoperative recovery was stable, and she was discharged four days later.

Histopathological examination of the uterine tissue, conducted one week post-surgery, revealed a tumorous mass characterized by a proliferation of endometrial glands forming tubular and acinar structures, partly arranged in a back-to-back pattern within the stroma. These glands were lined by atypical columnar epithelial cells with pleomorphic features, round-oval enlarged nuclei, coarse chromatin, and some with prominent nucleoli. The cytoplasm was eosinophilic and granular. Tumor infiltration was noted in less than half of the myometrium, with a solid non-glandular growth area measuring less than 5%. Evidence of blood vessel proliferation was observed, with some vessels showing signs of atherosclerosis, dilation, and congestion. However, no tumor cells were detected in the infiltrating blood vessels, and there was no lymphovascular space involvement.

The final histopathological diagnosis was low-grade endometrioid carcinoma of the uterine corpus associated with arteriovenous malformation. The patient was advised to undergo complete staging and additional treatment, but she declined further surgical intervention.

Discussion

ow-grade endometrioid carcinoma of the uterine corpus has been documented as a cause of secondary postpartum hemorrhage (PPH) in a case report (5). Another case involved a 28-year-old patient, similar in age to our patient, who presented with secondary PPH and was diagnosed with endometrial stromal sarcoma (6). Additionally, a case was reported of a 20-year-old primiparous woman who, six months post-vaginal delivery, was referred due to menometrorrhagia. A 5 cm mass

was identified on the anterior uterine wall during hysteroscopy, which was resected. The pathology report confirmed low-grade endometrial stromal sarcoma (7).

In our case, potential causes of secondary PPH, such as uterine atony, endometritis, and retained products of conception, were ruled out. Endometrial cancer developing during reproductive years and pregnancy is rare, as it typically occurs in postmenopausal women and is driven by estrogen. The elevated progesterone and reduced estrogen levels during pregnancy should theoretically prevent endometrial cancer development (1). Pregnancy may also inhibit the progression of hormone-sensitive cancers (8). In numerous cases reported in the literature, spontaneous miscarriage has occurred in pregnancies complicated by endometrial cancer (9). In our patient, there were no symptoms until 10 days post-vaginal delivery, when significant vaginal bleeding startedA review of 14 cases of postpartum endometrial cancer found that most patients lacked identified risk factors, with the median age being 32 years. Abnormal vaginal bleeding in the postpartum period was the most common symptom (4). Endometrial carcinoma is characterized by increased microvessel density compared to unaffected endometrium, linked to high levels of vascular endothelial growth factor (VEGF). VEGF plays a crucial role in both normal and pathological angiogenesis, lymphangiogenesis, and vasculogenesis. Rapid tumor growth, along with increased interstitial pressure and the greater distance between cancer cells and blood vessels, causes hypoxia. Hypoxia stimulates angiogenesis, leading to the formation of new blood vessels around the tumor, allowing it to receive oxygen and nutrients for continued growth (10).

Histologically, the source of bleeding can be attributed to multiple foci of necrosis within the malignant tissue, often associated with chronic endometritis in the surrounding stroma. Excessive epithelial proliferation, coupled with reduced peripheral blood flow, leads to hypoxia. The loss of endothelial integrity may cause vascular damage and bleeding. Necrosis of peripheral tissue, caused by the friction of the malignant mass within the uterine cavity, fragility of new blood vessels, and proteolytic enzymes from inflammatory cells, can also contribute to intermittent bleeding in cases of endometrial cancer (11). In our case, the depth of endometrial cancer likely explains the recurrent vaginal bleeding and secondary PPH.

Endometrial cancer is graded using two systems: the FIGO 3-grade assessment of glandular components and the binary histological grading system (low grade and high grade). Low-grade cancers have less than 50% solid components with no marked nuclear atypia, whereas high-grade cancers have over 50% solid components and/or significant nuclear atypia (12). The binary grading system is now preferred, as grade 1 and 2 tumors have similar prognoses, and combining these grades simplifies the classification process. Eliminating grade 2 from the current system may also improve risk stratification and reduce confusion regarding adjuvant therapy (13).

Vaccarello and Shiomi summarized 52 cases of pregnancies with endometrial cancer, with 48 of the cases being grade 1 or grade 2. This indicates that most endometrial cancers detected during pregnancy or the postpartum period are low-grade and carry a favorable prognosis (3, 14). A review of 14 cases of pregnancy-associated endometrial cancer found that 11 patients had low-grade disease, with 12 being FIGO stage 1. These patients underwent primary surgery and showed no signs of recurrence during follow-ups lasting 1 to 6 years (4).

Surgical treatment for endometrial cancer involves surgical staging, which includes total hysterectomy, bilateral salpingo-oophorectomy, and lymphadenectomy of the pelvic and para-aortic lymph nodes. The extent of surgery depends on clinical stage, histological type, and differentiation. Adjuvant therapy, including radiotherapy, chemotherapy, or hormonal treatments, is determined by clinical stage, histology, differentiation, and other risk factors. The five-year survival rate for low-grade endometrial cancer ranges from 69% to 90%. Studies report that the incidence of ovarian metastasis in clinical stage I endometrial cancer is about 5%. In our case, restaging is necessary as one ovary remains. Unfortunately, two years after the diagnosis, the patient still refuses complete surgery for staging or follow-up, although she has no current complaints (14).

Conclusion

In conclusion, this case highlights the rare occurrence of low-grade endometrioid carcinoma as a cause of secondary postpartum hemorrhage in a young woman, underscoring the need for heightened clinical awareness of endometrial cancer even in patients without typical risk factors. Despite the patient presenting with significant vaginal bleeding after delivery, the underlying malignancy was not initially suspected, demonstrating the importance of thorough evaluation in cases of unexplained postpartum hemorrhage. The histopathological findings confirmed the diagnosis, and while the prognosis for low-grade endometrial cancer is generally favorable, this case emphasizes the necessity for appropriate staging and management. Continued monitoring and potential follow-up treatments are crucial, as the patient's refusal of further surgical intervention highlights the challenges faced in managing such cases. This report serves as a reminder of the complexities involved in diagnosing and treating endometrial cancer during the reproductive years and the importance of individualized patient care.

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