RAPID PROGRESSION AND POOR PROGNOSIS IN ENDOMETRIOID OVARIAN CANCER ARISING FROM ENDOMETRIOMA: A CASE REPORT

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ABSTRACT

Endometriosis is linked to an increased risk of endometrioid ovarian cancer, though malignant transformation is rare. We report a 35-year-old nulliparous woman with a 12-year history of endometriosis who developed endometrioid ovarian cancer two months after her last surgery. Histological examination initially showed no malignancy, but subsequent immunohistochemical analysis confirmed cancer. The patient underwent surgery followed by six cycles of platinum-taxane chemotherapy. This case underscores the need for thorough assessment of patients in rapidly progressing endometriosis.

KEY WORDS: Endometriosis, Endometriosis-associated ovarian cancer

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INTRODUCTION

Endometriosis is a benign inflammatory disease that is characterized by the implantation of endometrium-like tissue outside the uterus in 5 to 15% of women of reproductive age[1]. It shares common features with the neoplastic process, including cancer-like cell invasion, rapid growth, angiogenesis, and a reduction in apoptosis[2]. In women with a long history of endometriosis, the relative risk of ovarian cancer is 40% higher compared with the control population[1]. Malignant changes in endometriosis affect approximately 0.1–1.6% of ovarian endometriomas. Endometrioid cancer represents the most well-known example of an epithelial malignancy arising from endometriosis. Patients with endometriosis-associated ovarian cancer (EAOC) are generally younger and have earlier-stage and low-grade disease compared to patients with de novo ovarian malignancies. In this case report, we present the malignant transformation of endometriosis to endometrioid ovarian cancer in a young patient with a poor prognosis. This paper aims to highlight the importance of comprehensive assessment in rapidly progressing and recurrent endometrioma to enable early detection of malignant transformation and improve patient outcomes.

Case Presentation

The patient is a 35-year-old nulliparous woman who has been treated for endometriosis at our hospital for 12 years. Initially, she had a cystectomy and left oophorectomy for a 15 cm endometrioma, followed by GnRH agonist injections. Eleven years later, she reported worsening abdominal pain. A multislice computed tomography (MSCT) revealed a septated pelvic mass from the right ovary, approximately 11.4 × 8.2 cm axially and 8.7 × 11 cm coronally, diagnosed as a recurrent endometrioma. She was prescribed dienogest 2 mg.

Six months later, she experienced acute abdominal pain and visited the emergency unit. An MRI suggested a ruptured ovarian endometrioma, leading to an emergency laparotomy. During surgery, a 10 cm right endometrioma was identified, with brownish fluid confirming the rupture. A cystectomy was performed, preserving the right ovarian tissue to maintain fertility. Histopathology of the ruptured cyst showed fibrous tissue, simple cuboidal-columnar epithelium, hemorrhages, and hemosiderophages, without signs of malignancy, confirming external endometriosis.

Two months later, she returned to the emergency unit, complaining of severe abdominal pain not alleviated by painkillers. A mass as high as the umbilicus was palpable, and an MSCT showed an inhomogeneous lesion in the right ovary, with irregular edges, measuring 10.4 × 9.3 × 11.7 cm, with papillary projection and septations, infiltrating the superior wall of the bladder with para-aortic lymph node metastases and ascites. Laparoscopic surgery was then planned. During the surgery, a right ovarian cyst measuring 12 cm in diameter was discovered. It was adherent to the omentum, intestine, and anterior abdominal wall. Adhesiolysis was performed, and the cyst was subsequently ruptured. Cystic fluid was aspirated, a papilla seen inside the cystic mass, and cyst capsule were sampled.

Pathological examination showed ovarian tissue with back-to-back tubular and papillary formations, along with solid tumors. Some areas exhibited squamous metaplasia ("squamous morules"). Tumor cells were polymorphic, partially columnar and ciliated, with eosinophilic, clear, and vacuolated cytoplasm. The nuclei were round-oval, poorly polarized, with irregular membranes, rough chromatin, and visible nucleoli. The stroma was oedematous with dilated vessels, hemorrhage, and extensive necrosis. Peritumoral lymphocytic infiltration was about 1%. The diagnosis was endometrioid carcinoma, FIGO grade 1. The cyst capsule showed ovarian tissue without tumor involvement and areas of dilated endometrial glands surrounded by endometrial stroma, infiltrated by lymphocytes, histiocytes, and hemosiderophages. The capsule and cortex exhibited external endometriosis.

Following the pathology result, surgical staging was performed, revealing another mass originating from the right ovary, measuring 15 cm in diameter. Total abdominal hysterectomy, right salpingo-oophorectomy, and omentectomy were conducted. Pathological study confirmed endometrioid carcinoma in the right ovary, and no malignancies were found in other organs. The patient was then diagnosed with endometrioid ovarian carcinoma stage IC3, FIGO grade 1. Based on this finding, immunohistochemistry (IHC) staining using p53, Ki57, and estrogen receptor (ER) markers was performed on the previous endometriosis pathology slides from the last endometrioma samples and pathology slide of endometrioid ovarian cancer samples, to investigate the malignancy transformation of endometriosis (Figure 1).

The IHC study on endometriosis samples revealed that ER staining was strongly positive in most of the nuclei of lining epithelial cells. P53 staining was also strongly positive in most nuclei of lining epithelial cells, while Ki-67 was positively stained in approximately 70% of these nuclei. In another IHC study of endometrioid ovarian cancer samples, ER staining was strongly positive in most tumor cell nuclei. P53 showed moderate intensity staining in a small portion of tumor cells, and Ki-67 was positive with strong intensity in approximately 85% of tumor cells. These findings for the right ovarian tumor were consistent with a diagnosis of endometrioid carcinoma, FIGO grade 1, with a proliferation index of approximately 85%, which suggested a malignant transformation of endometriosis to endometrioid ovarian cancer.

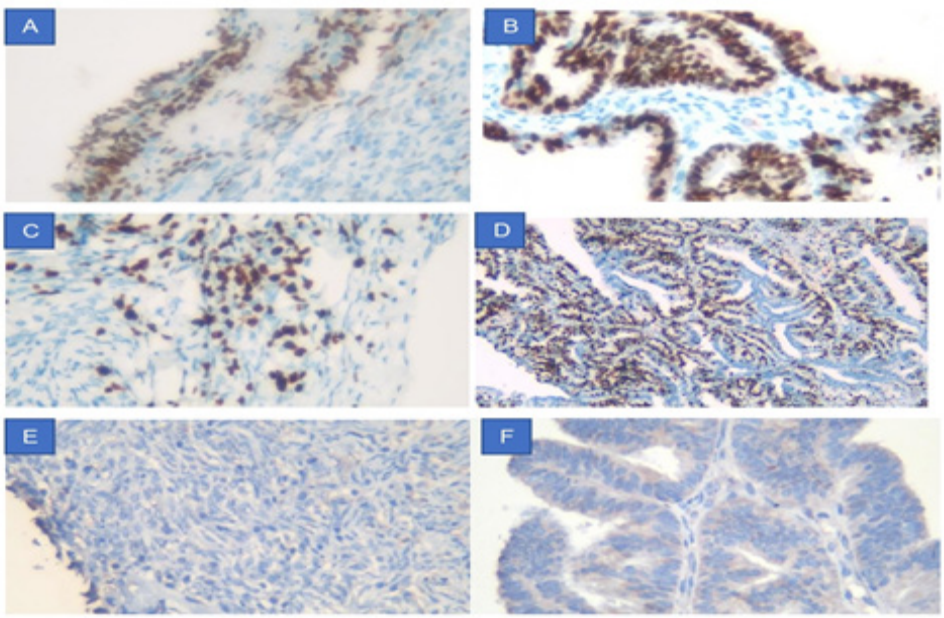

Figure 1. Immunohistochemical staining of ER, Ki67, and P53 in endometrioma and ovarian endometrioid carcinoma. (A) ER shows strong positive staining in the nuclei of lining epithelial cells in endometrioma. (B) ER is similarly stained in ovarian endometrioid carcinoma. (C) Ki67 is positive in approximately 70% of the nuclei of lining epithelial cells in endometrioma, while (D) 85% of the nuclei are positive in ovarian endometrioid carcinoma. (E) P53 displays strong positive staining in the nuclei of lining epithelial cells in endometrioma. (F) In ovarian endometrioid carcinoma, P53 is stained with moderate intensity in a small portion of tumor cell nuclei.

The patient received platinum- and taxane-based chemotherapy for six cycles following surgical staging. However, she relapsed 14 months later, with pleural cytology suggesting metastatic carcinoma of the ovary. A subsequent abdominal MSCT showed an inhomogeneous mass in the left parametrium, measuring approximately 7.2 × 8.2 × 8.9 cm, with papillary projection and septation, infiltrating the superior wall of the urinary bladder. She then underwent second-line chemotherapy with cyclophosphamide, doxorubicin, and cisplatin. Before the sixth cycle, her condition deteriorated. She experienced severe headaches and lost her vision, with an acute infarct in the bilateral occipital and bilateral cerebellum lobes found on brain MRI. Coagulation factors were abnormal, with a platelet count of 96,000/µL, an INR of 1.13, a D-dimer of 20,227 ng/mL FEU, and a fibrinogen level of 115 mg/dL. Three weeks later, she had respiratory distress and was transferred to the ICU due to pneumonic-type metastases and pulmonary edema. She died a month later due to septic shock.

Discussion

EAOC is rare, estimated to occur in about 0.1–1.6% of women with endometriosis[3]. The main histological types of EAOC are endometrioid adenocarcinoma and clear cell carcinoma[4]. EAOC usually presents in women 10 to 20 years younger and has a better prognosis than de novo ovarian cancer. The risk of developing EAOC is increased, particularly in women with a long history of endometriosis, especially those whose disease duration exceeds ten years from initial diagnosis[5]. In a 10-year retrospective analysis in Taiwan, all the patients who developed EAOC were above 40 years old (3). Interestingly, in our case, the patient was 35 years old, which is approximately 5 years younger than the respective study.

EAOC is characterized as the development of ovarian cancer in the ipsilateral or contralateral ovarian endometriosis or pelvic endometriosis, with histological findings compatible with an endometrial origin. It requires the absence of primary tumor sites and histopathological evidence of transition from benign endometriosis to malignant tumor[4,6]. This latter aspect poses a challenge in the clinical setting, as benign epithelial tissues in endometriosis are often replaced by malignant lesions. However, in our case, the endometriosis tissue was present alongside the endometrioid ovarian cancer, which confirms the EAOC diagnosis.

EAOC is typically associated with early-stage and low-grade disease[1], which aligns with our case, as our patient was diagnosed with endometrioid ovarian carcinoma stage IC3, FIGO grade 1. Early diagnosis of EAOC may be attributed to symptoms related to endometriosis, including dysmenorrhea, chronic pelvic pain, dyspareunia, or new onset of lower abdominal bloating. A study found that more than 70% of 33 patients experienced malignant transformation within a decade of monitoring their endometriomas[7]. In our case, the patient was diagnosed with endometrioid ovarian cancer twelve years after her initial diagnosis of endometriosis.

Factors contributing to the development of EAOC include molecular genomic alterations, oxidative stress, inflammation, and hormonal influences such as hyperestrogenism[6]. However, currently, no single biomarker can predict the malignant transformation of endometriosis. A recent systematic review revealed altered expression in the phosphoinositide 3-kinase (PI3K)/AKT/mTOR pathway, p53, ARID1a, estrogen and progesterone receptors, transcriptional, nuclear, and growth factors in atypical endometrioma compared to endometriosis[8]. In this report, we used Ki-67, ER, and p53 to investigate the malignant transformation of endometriosis into EAOC. Ki-67 can be used to predict the premalignant potential of atypical endometriosis, as its expression increases from endometriosis to atypical endometriosis and eventually to cancer, which is consistent with our case. A study showed no difference between p53 staining of invasive EAOC and its precursor lesion[9]. Our IHC study showed different results, where p53 staining is stronger in endometriosis compared to EAOC. Marked p53 expression in benign

endometriosis with weaker staining in malignant tissues represents an unusual pattern, potentially indicating non-pathogenic protein accumulation or wild-type overexpression unrelated to mutation. According to a study, low p53 staining is associated with a more favorable prognosis of endometrioid ovarian cancer. However, in our case, the disease was rapidly progressing and the prognosis remains poor. This could be explained by other mutations such as mismatch repair proteins (MMR) and polymerase ε (POLE) exonuclease domain mutations, which contribute to carcinogenesis and tumor progression[10]. A previous study demonstrated higher ER expression in EAOC compared to endometriosis[11]. In contrast, in our case, ER expression was similarly strong in both the endometriosis foci and the cancerous tissue samples. Our IHC study indicates the possibility of malignant changes of endometriosis since there was a high proliferation index in the endometriosis tissue, strong positive ER staining, and strong p53 staining, although no cell atypia was found in the pathology examination.

The management strategies for EAOC and de novo ovarian cancer are similar, involving complete surgical intervention, either by primary cytoreductive surgery or by interval cytoreductive surgery, followed by platinum-taxane-based chemotherapy. The 10-year survival rate of EAOC is 90%[3]. Our patient died two years after the cancer diagnosis, despite an early-stage diagnosis, partly due to chemotherapy-related coagulopathy[12]. This case is unique due to the rapid growth and poor prognosis of EAOC, which differ from those described in the existing literature. EAOC typically evolves gradually from pre-existing benign endometriotic lesions to atypical endometriosis to invasive carcinoma over several years[5]. In this case, the diagnosis shifted from endometrioma to endometrioid ovarian cancer within just two months based on the pathologic findings, although the possibility of cellular atypia in the endometriosis sample cannot be excluded. Fertility-sparing surgery was initially planned despite the sign of malignancy found during ultrasound examination, which then delayed the complete surgical staging by about a month. This could have contributed to the delay in more aggressive treatment. The significant size and persistent endometriosis, along with the rapid enlargement of the ovarian mass, raise concerns and necessitate both surgical intervention and thorough pathological assessment.

Conclusions

This case reveals a rare, rapidly progressing EAOC in a younger patient. Despite an early-stage diagnosis, aggressive histopathology makes the prognosis remain poor. The abrupt shift from benign endometrioma to carcinoma underscores the need for vigilant long-term monitoring and careful histopathology assessment in persistent endometriosis beyond ten years. Tailored diagnostic protocols may improve outcomes in atypical EAOC presentations.

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Ethics approval

Our institution does not require ethics approval for reporting individual case reports. However, the patient gave informed consent for the procedure, publication of this case report, and accompanying images. Patient identity is not disclosed. Written informed consent was obtained from the patient's guardian.

Contributions

RW, AB, SW, and AK drafted, designed, planned, organized, and interpreted the case study and manuscript writing. SW and AK contributed to the care of the patient and reviewed the report critically. All the authors approved the version to be published and agreed to be accountable for all aspects of the work in ensuring that questions

related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Competing interests
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