

Synchronous occurrence of primary right ovarian endometrioid adenocarcinoma and primary left ovarian clear cell adenocarcinoma

A case report

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Abstract

Rationale: Ovarian malignancy is associated with one of the highest rates of death among gynecological reproductive system malignancies. While progress has been made in surgical and postoperative adjuvant treatment approaches, the early atypical clinical manifestations, quick progression, and lack of the effective early screening means imply that the prognosis remains poor. Bilateral ovarian cancers are common, but different types of primary bilateral ovarian carcinomas are extremely rare.

Patient concerns: According to clinical pathologic, immunohistochemistry, and medical imaging data, a 51-year-old Chinese woman with abdominal pain was diagnosed as having right ovarian well-differentiated endometrioid adenocarcinoma with mucinous adenocarcinoma and left ovarian clear cell adenocarcinoma.

Diagnoses: Immunohistochemistry confirmed the diagnosis of primary bilateral ovarian cancers.

Interventions: She received multimodal treatment including surgery and chemotherapy.

Outcomes: The patient's recovery was uneventful, and she responded well to the chemotherapy.

Lessons: We speculate that the different types of primary bilateral ovarian carcinomas presented in this case may be due to different malignant transformations of the endometriotic lesions. Therefore, clinicians should pay special attention to the possible malignant transformation of endometriosis.

Abbreviations: CA = carbohydrate antigen, EM = endometriosis, ER = estrogen receptor, OCCA = ovarian clear cell adenocarcinoma, PR = progesterone receptor.

Keywords: endometriosis, immunohistochemistry, ovarian carcinoma, primary ovarian carcinoma

1. Introduction

There are many types of ovarian cancer. Ovarian endometrial cancer accounts for 10% of ovarian epithelial tumors; immunohistochemical studies have shown that ectopic lesions and cancer lesions are positive for the estrogen receptor (ER) and progesterone receptor (PR), indicating a relatively higher level of ER stimulation, which can promote disease development.^[1] Ovarian clear cell carcinoma is associated with a high mortality rate and is a highly malignant tumor closely associated with

endometriosis (EM).^[2,3] EM is a chronic disease affected by genetic, epigenetic, and environmental and ethnic factors; although EM does not belong to the categorization of precancerous disease, its epidemiology, pathology, molecular genetics, and etiology indicate that it has malignant potential. EM lesions are extensive and morphologically diverse; have malignant biological behavior, such as infiltration, metastasis, and recurrence; can infiltrate and damage tissues; promote angiogenesis; and spread to distant organs.^[4] Studies have shown that approximately 1% of patients with EM will harbor a malignancy, with the most common site being the ovaries.^[5] Adenocarcinoma and sarcoma are among the common types of malignant endometriotic lesions, and the most ovarian pathologies are endometrioid carcinoma and clear cell carcinoma.^[6] In 1925, Sampson first reported the phenomenon of malignant transformation of EM into ovarian cancer.^[7]

We report a case of primary bilateral ovarian cancers of different types and report their immunohistochemical results for the first time.

2. Case report

The patient provided informed consent to publish her case.

A 51-year-old menopausal, Chinese woman who presented with abdominal pain visited another hospital and underwent emergency surgery for suspicion of ovarian cyst rupture. She underwent a right-sided salpingo-oophorectomy in August 2016 (the specific operative procedure is unknown). The pathological results indicated ovarian cancer. Our hospital's pathology

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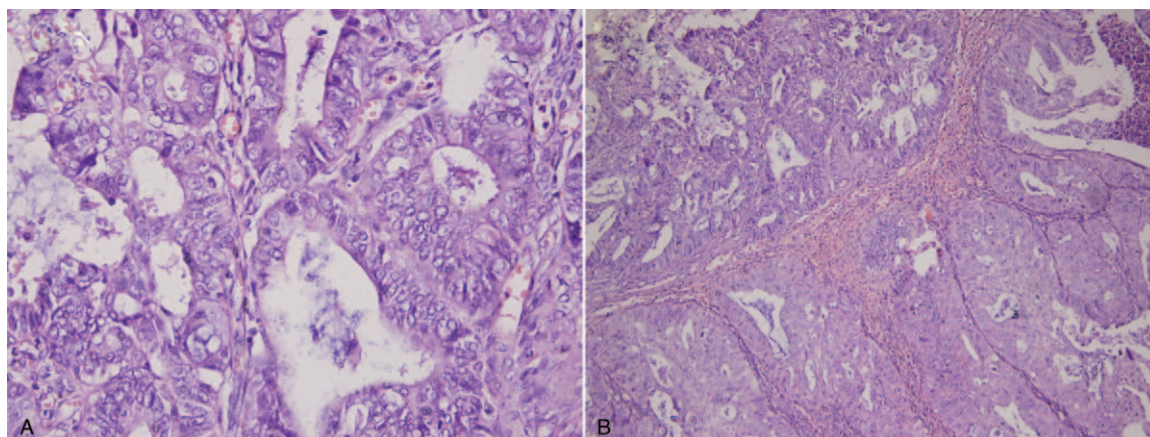


Figure 1. (A) Right ovarian endometrioid adenocarcinoma (hematoxylin–eosin stain $\times 400$), (B) right ovarian endometrioid adenocarcinoma (hematoxylin–eosin stain $\times 100$).

department was consulted and found that the specimen from the right salpingo-oophorectomy had a highly differentiated endometrioid adenocarcinoma with mucinous adenocarcinoma differentiation and multiple lesions (Fig. 1).

The patient was transferred to our hospital for further treatment. The specialist's examination found that she was married and had a child. The vulva showed normal development. The vagina was unobstructed, and the cervical mast cells were smooth. The uterine body was in the former position with a normal size and poor activity. The gynecological examination showed thickening of the left side and a lack of tenderness. The levels of carbohydrate antigen (CA)-199 and carcinoembryonic antigen were within normal limits, but the CA-125 level was increased to 63.7 U/mL (normal, <35 U/mL).

The gynecological sonogram showed the following. The posterior uterus measured 3.3 cm \times 4.3 cm \times 4.2 cm. The right adnexa had a weak echo, similar to a cyst, with no agent or blood flow signals, and measured 3.0 cm \times 1.9 cm \times 2.5 cm. There was no obvious free liquid dark area in the pelvic cavity. An enhanced scan of the abdominal basin (total abdomen) showed the following: First, behind the right side of the uterus, there was a 2.0 \times 3.5 cm cystic shadow, the surrounding fat gap was increased but blurry, and posterior wall of the uterus had unclear boundaries with thickening at both sites of attachment. Second, no ascites or thickening of the omentum was observed. Third, the abdominal and pelvic aorta were increased in size without any obvious lymph nodes. Fourth, the liver and kidneys had a few small densities and cysts; the gallbladder, spleen, and pancreas had no abnormalities. Scanning within the left upper lobe under the tongue and the middle right lung showed chronic infection. The cardiac ultrasonogram, chest radiograph, electrocardiogram, and other tests indicated no other abnormalities. We made a preliminary diagnosis of adenocarcinoma of the ovary with highly differentiated endometrioid adenocarcinoma, mucinous adenocarcinoma differentiation, and multifocal squamous metaplasia after resection of the right accessory.

Then the patient underwent abdominal hysterectomy and left attachment resection, pelvic and abdominal aortic lymph node dissection, omentum resection, appendectomy, intestinal adhesiolysis, and ureteral adhesiolysis in October 2016. The operation was difficult to perform, but it was uneventful.

Postoperative pathologic examination showed malignant transformation of the endometrial cysts and formation of clear cell carcinomas within, and confined to, the left ovary (Fig. 2). Immunohistochemistry showed positive expressions of CD15 and CK7; negative expression of CK20; focal positive or weak positive expression of napsin A, P53, ER, and PR, and positive expression of PAS. The Ki-67 labeling index was 55%, which supported the diagnosis (Fig. 3). The uterus, both fallopian tubes, and the appendix showed no obvious abnormalities. There was no lymph node metastasis observed. The surgical margin from left and right lateral pelvic wall surgery showed no cancer involvement, although the right surgical margin had the endometriotic lesions (Fig. 2G). Based on these findings, in combination with the preoperative histological findings of the right ovary, we believed that the left ovarian clear cell adenocarcinoma (OCCA) had developed independently. Therefore, the patient was diagnosed with primary bilateral ovarian cancers. Postoperatively, the patient was transferred to the chemotherapy ward and received a total of 5 cycles of paclitaxel–carboplatin chemotherapy. During the 1-year follow-up period, she examined blood tumor markers regularly and recovered well.

3. Discussion

Ovarian cancer is a common malignancy of the female reproductive system, but it is also associated with the highest mortality rate among gynecological malignancies due to the lack of understanding of precancerous lesions of ovarian cancer and the absence of early screening of ovarian cancer; therefore, most patients are diagnosed late. Thus, the prognosis of ovarian cancer is poor; the 5-year survival rate is less than 40%.^[8] Statistical literature on bilateral ovarian cancers reported an incidence of about 48.8% to 50%. While bilateral ovarian cancers can occur independently, the development of different pathological types is an extremely rare situation, and no domestic or international studies have previously reported it.

Our case of right ovarian well-differentiated endometrioid adenocarcinoma with mucinous adenocarcinoma, clear cell adenocarcinoma of the left ovary, and involvement of the left and right ovaries is an example of primary bilateral cancers. Ovarian endometrioid adenocarcinoma is a rare pathological type of ovarian malignancy, accounting for about 6.4% of cases,

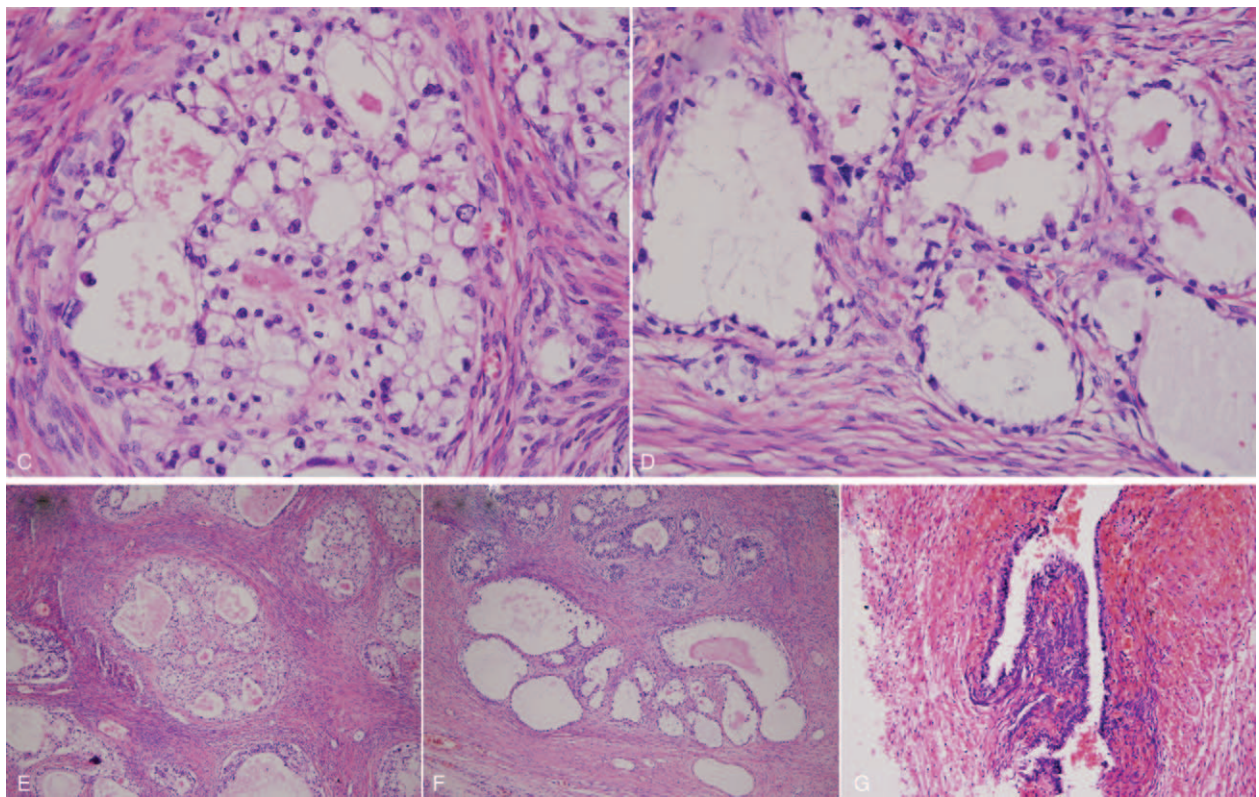


Figure 2. (C and D) Left ovarian clear cell carcinoma (hematoxylin–eosin stain $\times 400$), (E and F) left ovarian clear cell carcinoma (hematoxylin–eosin stain $\times 100$), (G) left ovarian endometrial cyst lesion area (hematoxylin–eosin stain $\times 200$).

and it is moderately malignant. There are 2 different hypotheses on the histological origin of ovarian endometrioid adenocarcinoma: one is that ovarian germinal epithelium leads to endometrial differentiation, and the second is that the malignant

transformation of EM may lead to its occurrence. OCCA has the highest mortality rate among all gynecological malignancies.^[9] In 1973, the World Health Organization confirmed that OCCA was an independent clinical subtype of ovarian epithelial cancer, and

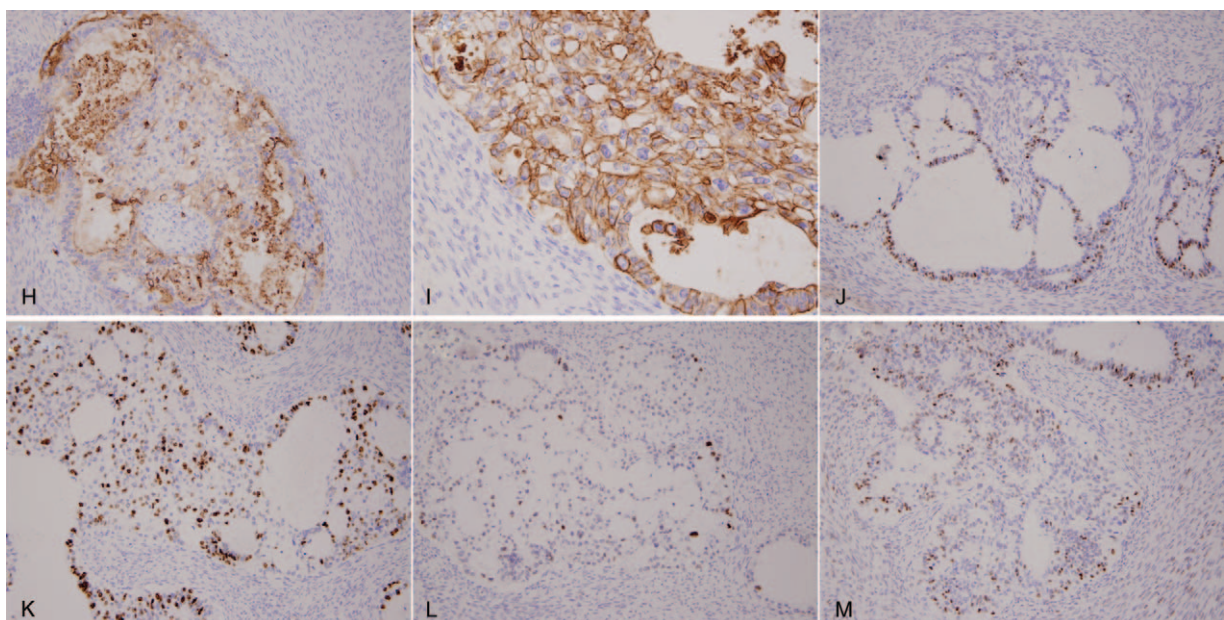


Figure 3. Immunocytochemistry for (H) CD15, (I) CK7, (J) estrogen receptor, (K) Ki-67, (L) P53, and (M) progesterone receptor.

its 5-year survival rate is still below 50%.^[10] Up to 25% to 55% of OCCA patients have EM, and in some cases, a transition from EM to atypical EM or pathological changes indicating transition to clear cell carcinoma can be seen; therefore, some scholars believe that at least part of OCCA is derived from malignant EM.^[11] Considering how some cases occur in patients with a history of dysmenorrhea associated with increased menstrual flow, and the fact that the right surgical margin often contains endometriotic lesions, it is speculated that the development of primary ovarian cancer may be related to the extent of malignant transformation in endometriotic lesions.

The current patient had a rare disease associated with a high degree of malignancy, risk of relapse, and poor prognosis; therefore, similar patients should be diagnosed as early as possible to achieve effective treatment. Before diagnosing this rare disease, mutual metastasis or direct infiltration of bilateral ovarian cancers must be ruled out. Ovarian cancer can be transferred to the contralateral ovary, and some literatures have reported an incidence of up to 25%.^[12] Patients with the preoperative, morphological, and immunohistochemical findings similar to our patient may have primary bilateral cancers. At the same time, it is necessary to confirm the source of the tumor, excluding retroperitoneal tumors, sigmoid colon tumors, and rectal cancer. B-ultrasonography, barium enema examination, and sigmoidoscopy can help identify the source.

A study showed that about 1% of women with EM have lesions that undergo malignant transformation, with the main site being the ovary, and that the risk of epithelial ovarian cancers, such as ovarian endometrioid carcinoma and clear cell carcinoma, increased but that of high-grade serous and mucinous cancers did not.^[13] Therefore, surgeons should carefully consider treatment for postmenopausal patients with EM and those with EM and ovarian cysts (>10 cm in diameter).^[14] The standard treatment of primary bilateral ovarian cancers remains surgery supplemented by radiotherapy, chemotherapy, and other supportive treatments. In our case, the patient's chemotherapy protocol was chosen based on the postoperative pathological results of bilateral ovarian cancer. The patient received a total of 5 cycles of paclitaxel-carboplatin chemotherapy. During the 1-year follow-up period, she examined blood tumor markers regularly and recovered well.

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