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ABOUT COVER

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CASE REPORT

Endometriosis-associated endometrioid adenocarcinoma of the fallopian tube synchronized with endometrial adenocarcinoma: A case report

Jian-Yang Feng, Qing-Ping Jiang, Hong He

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Abstract

BACKGROUND

Endometriosis is a common gynecological disorder that affects women of reproductive age. It is characterized by a cancer-like invasion of the extra-uterine endometrium and exhibits a strong association with ovarian clear cell cancer and endometrioid cancer. Endometriosis-associated fallopian tube endometrioid adenocarcinoma synchronized with endometrial adenocarcinoma was rarely reported.

CASE SUMMARY

A 49-year-old woman was referred to our hospital complaining about abnormal vaginal bleeding for three years following unsatisfactory medication. Intraoperative frozen sections unexpectedly unveiled an endometrioid cancer of the left fallopian tube with superficial invasion surrounded by diffuse endometriosis synchronized with endometrioid endometrial cancer.

CONCLUSION

It was difficult to make a differential diagnosis when confronted with incidental findings of fallopian tube cancer lesions synchronized with endometrial cancer. The key differential diagnosis of primary endometriosis-associated endometrioid adenocarcinoma of the fallopian tube from endometrial adenocarcinoma involvement relies on the pathological identification of malignant transformation in fallopian tube endometriosis disease.

Key Words: Endometriosis-associated cancer; Fallopian tube neoplasms; Endometrial neoplasms; Case report

Core Tip: The key to distinguishing primary endometriosis-associated fallopian tube cancer from fallopian tube involvement in endometrial cancer was the pathological identification of malignant transformation in endometriosis-associated fallopian tube tumors.

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INTRODUCTION

Endometriosis is a common gynecologic, estrogen-dependent, and benign chronic inflammatory disease caused by ectopic endometrial-tissue infiltration with three heterogeneous phenotypes (superficial endometriosis, ovarian endometrioma, and deep infiltrating endometriosis)[1]. Possible causes for endometriosis involve retrograde menstruation, pre-existing endometrial abnormalities, and inflammatory factors[1,2]. There is evidence for endometriosis exhibiting a potential for malignant transformation, and that this change can constitute a precursor lesion of ovarian clear cell cancer and endometrioid cancer[3,4]. However, the mechanism(s) underlying the carcinogenesis of endometriosis requires further elucidation. According to the most recent staging system of the International Federation of Gynecology and Obstetrics (FIGO), fallopian tube involvement of endometrial cancer should be staged as FIGO IIIa, while synchronized primary endometrial cancer and primary fallopian cancer should be staged respectively. Under some circumstances, however, it is difficult to make a differential diagnosis, *e.g.*, when confronted with incidental findings of fallopian tube cancer lesions synchronized with endometrial cancer. It was therefore critical to our case to identify the origin of the cancerous lesion, and thus contribute to the determination of cancer stage and post-operative therapeutic options. This report was approved by the hospital ethics committee (approval number: 2022-009).

CASE PRESENTATION

Chief complaints

A 49-year-old woman, gravida 1 and para 0, complained about abnormal vaginal bleeding for three years.

History of present illness

Her last menstrual period had been 2019-2-19, and her bleeding during it was slight, irregular, and intermittent. Bleeding began during the menstrual interval and lasted for a short period without other concomitant symptoms. She was prescribed 10 mg of dydrogesterone twice a day for 10–14 days to relieve symptoms for a few months, but the results were unsatisfactory. Transvaginal sonography indicated a 22.0-mm thick endometrium with a non-homogeneous echo pattern, and further diagnostic curettage was then performed. The pathology report ultimately identified local, atypical complex hyperplasia of the endometrium.

History of past illness

There was no other illness in previous medical history.

Personal and family history

We noted no exceptional other personal and family history.

Physical examination

Physical examination showed that her BMI was 27.89 kg/m^2 (weight, 67 kg; height, 155 cm), and bimanual palpation showed an active and painless mass of approximately 40.0 mm at the left adnexa with no other positive findings.

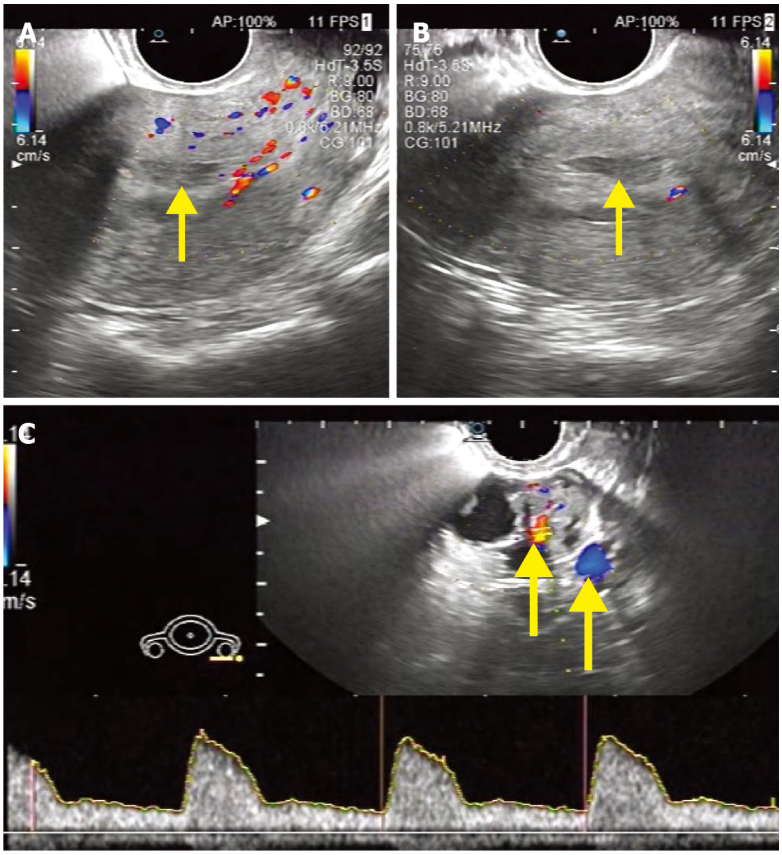

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Figure 1 Transvaginal ultrasonographic examination of the uterine cavity and fallopian tube. A and B: Transvaginal sonography indicates a mixed lesion (A–B) with a non-homogeneous echo (yellow arrow) in the uterine cavity and a solid cyst (yellow arrow) (C) of the left adnexa; both lesions are accompanied by a rich blood flow. A low resistance index (RI, 0.78) and high arterial spectrum (Vmax, 26 cm/s) of the left adnexal mass (yellow arrow) are also detected.

Laboratory examinations

Laboratory tests indicated a hemoglobin level of 117 g/L (range, 115–150), and some serum tumor markers were unremarkable: CA125 of 17.0 u/mL (range, 0–47), CA153 of 7.2 U/mL (range, 0–20), CA199 of 15.51 U/mL (range, 0–43); however, HE4 (110.4 pmol/L; range, 29.3–68.5) was slightly increased. Liver, kidney, and coagulation functions were negative, and the liquid-based cytology and high-risk HPV tests were negative.

Imaging examinations

Transvaginal ultrasonography revealed a uterine volume of 63.0 mm × 51.0 mm × 58.0 mm, a mixed lesion (33.0 mm × 14.0 mm) with a non-homogeneous echo in the uterine cavity, and a solid cystic mass (50.0 mm × 29.0 mm) of the left adnexa (Figure 1A-C).

A pathological review at our hospital suggested that the mass of the uterine cavity was a local, atypical, and complex endometrial hyperplastic lesion.

FURTHER DIAGNOSTIC WORK-UP

The patient had no desire to preserve her uterus and a malignant endometrial lesion had not been completely excluded within the context of a local, atypical, and complex endometrial hyperplastic lesion. After completing the preoperative examination to exclude operative contraindications, laparoscopic surgery was scheduled with full informed consent. Surgical exploration displayed a distorted and thickened left hydrosalpinx (50.0 mm × 40.0 mm) with a blocked end (Figure 2A). When we viewed the serous-membrane surface of the left fallopian tube we observed no suspected lesions, and we also suspected there were none in the left ovary, right adnexa, or the surface of the uterine body. Total hysterectomy and bilateral salpingo-oophorectomy were then performed. We thus uncovered incidental cauliflower lesions and fish-like exogenous lesions filled with a feculent liquid in the left tube by sectioning the lesions intraoperatively (Figure 2B) and found an ulcerous lesion of the endometrium (20.0 mm × 10.0 mm) in the left uterine horn (Figure 2C). Frozen sections unexpectedly unveiled a left fallopian tube endometrioid cancer with superficial myometrial invasion surrounded by diffuse

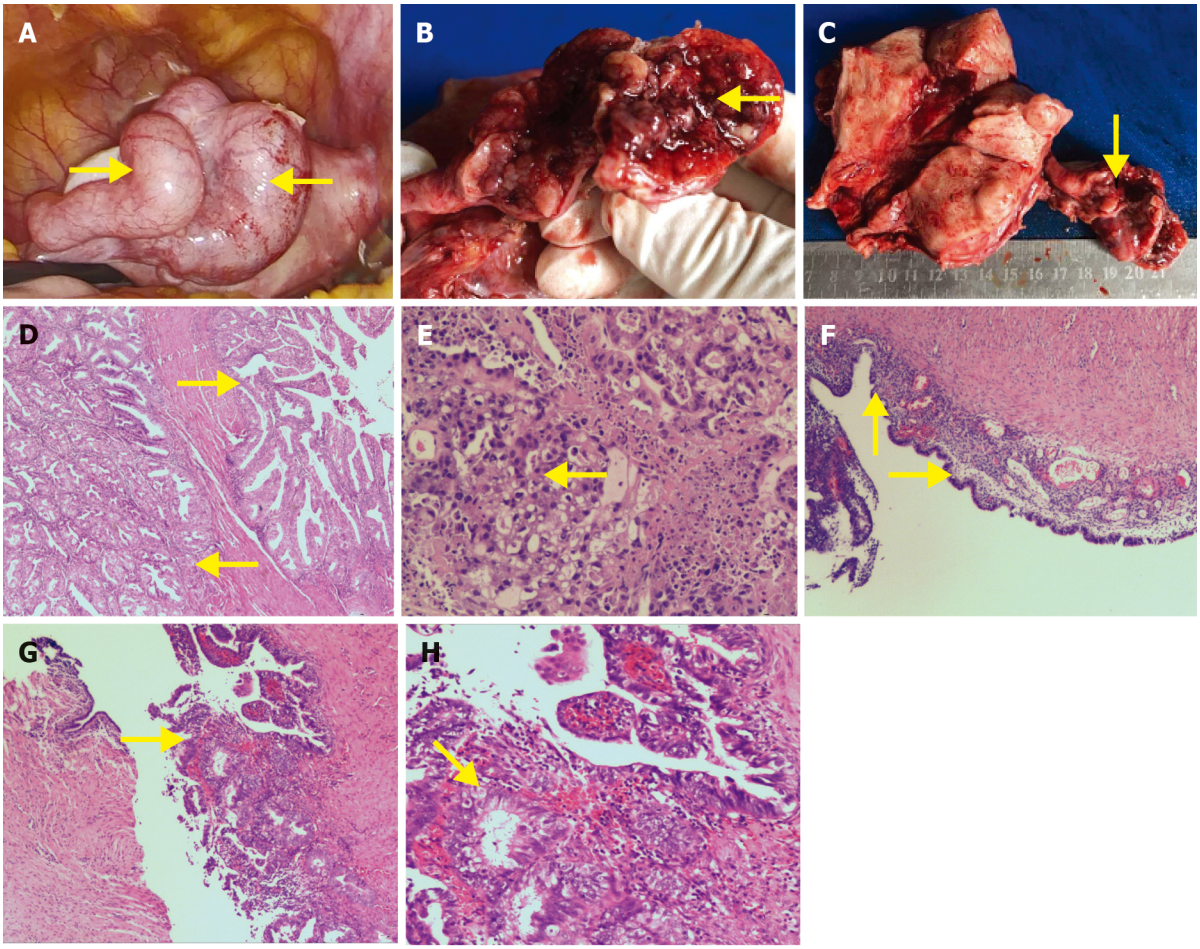

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Figure 2 Fallopian tube endometrioid adenocarcinoma arising from endometriosis synchronized with endometrial endometrioid adenocarcinoma. A: A distorted and thickened left hydrosalpinx (50.0 mm × 40.0 mm) with a blocked end (yellow arrow) was seen during laparoscopic exploration; B: Diffuse, cauliflower, and fish-like exogenous cancerous lesions (yellow arrow) were filled with feculent liquid in the left fallopian tube; C and D: The endometrioid adenocarcinoma in the uterus was grade 1, with a myometrial invasion of less than 50% (Hematoxylin-eosin Staining, HE, ×100, yellow arrow); E: Endometrioid adenocarcinoma of the fallopian tube (HE, ×100, yellow arrow); F: The endometriotic area in the mucosa of the left fallopian tube (HE, ×100, yellow arrow); G and H: The transitional area from endometriosis to atypical hyperplasia in the left fallopian tube (G, HE, ×100; H, HE, ×200, yellow arrow).

endometriosis synchronized with endometrioid endometrial cancer. We then implemented complete staging surgery, including bilateral pelvic and para-aortic lymphadenectomy.

Final paraffin pathology confirmed a well-differentiated endometrial endometrioid adenocarcinoma (EEA) derived from the uterine fundus with myometrial invasion of less than 50% (Figure 2D), positive left parametrial metastasis, and negative lymphovascular space involvement or pelvic and para-aortic lymphadenopathy. We also simultaneously diagnosed an endometriosis-associated endometrioid adenocarcinoma of the left fallopian tube (Figure 2E) and detected a transitional area from the endometriosis to the atypical hyperplasia to endometrioid adenocarcinoma in the left fallopian tube (shown in Figure 2F, 2G, and 2H). These two cancerous lesions also shared similar expression patterns for ER-α, PR, P53, Ki-67, PTEN (Figure 3A and 3C), PAX2 (Figure 3B and 3D), WT-1, MLH1, MSH2, MSH6, and PMS2 upon immunohistochemical examination.

FINAL DIAGNOSIS

After discussion by a multi-disciplinary team, we concluded it was a simultaneous FIGO I stage endometriosis-associated fallopian tube endometrioid adenocarcinoma and FIGO IIIb stage EEA.

TREATMENT

Since a high-risk clinicopathological factor–positive left parametrial metastasis was identified,

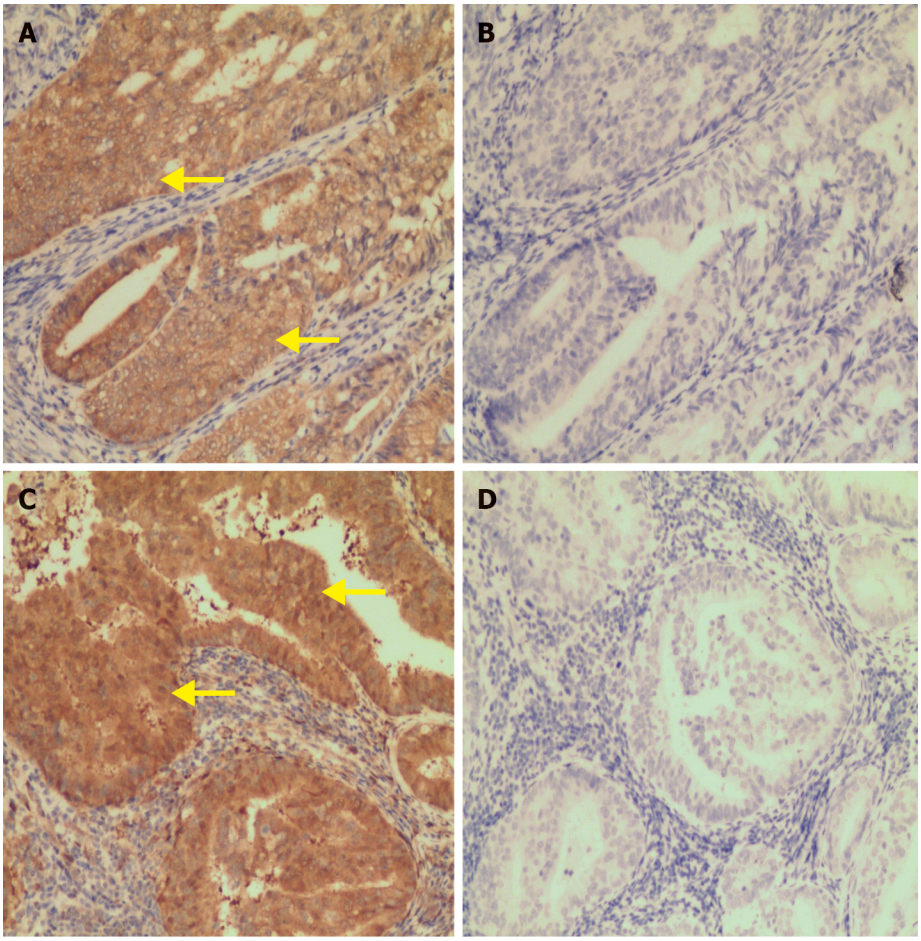

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Figure 3 PTEN and PAX2 expression patterns in endometrial and fallopian tube endometrioid adenocarcinoma. Both endometrial- and fallopian-tube endometrioid adenocarcinoma showed the same model for positive expression of PTEN (A and C, IHC, ×100, yellow arrow) and loss of expression of PAX2 (B and D, IHC, ×100).

postoperative adjuvant pelvic external beam radiotherapy and brachytherapy were prescribed.

OUTCOME AND FOLLOW-UP

Postoperative routine follow-up was performed. The results of postoperative dynamic HE-4 examination, vaginal stump cytology, and pelvic and abdominal sonography were negative. There was no evidence of recurrence in the subsequent three years.

DISCUSSION

Endometriosis is a condition in which functional endometrial tissue is present outside the uterus, and it is associated with an increased risk of ovarian and endometrial cancer[5]. Endometriosis is often confined to the pelvic cavity and principally involves the ovary, ovarian ligaments, cul-de-sac, and uterovesicular peritoneum; however, with a preoperative diagnosis of endometriosis in patients undergoing laparoscopic surgery, the incidence of fallopian tube endometriosis was 3.8%–12% macroscopically and 37.4–42.5% microscopically[6]. The most common histological subtype of malignant transformation in endometriosis is clear cell cancer, followed by endometrioid adenocarcinoma[7], with age-adjusted incidence ratios of 2.29 [95% confidence interval (CI): 1.24–4.20] for ovarian clear-cell cancer and 2.56 (95%CI: 1.47–4.47) for endometrioid ovarian cancer[8]. Importantly, the incidence of microscopic fallopian tube endometriosis among patients with histologically diagnosed endometriosis was significantly higher than in those manifesting macroscopic disease (42% *vs* 11%–12%, respectively)[6]. Ectopic endometriotic lesions are, in theory, estrogen-dependent and can invade the stroma, demonstrating their potential for malignant transformation. However, the prognostic impact of endometriosis on endometriosis-associated cancers is elusive[7,9,10].

In this case, we first noted the marked evolutionary malignant transformation from fallopian tube endometriosis to atypical hyperplasia to endometrioid adenocarcinoma. We hypothesized that the stimuli required to promote the malignant transformation were non-ovarian-derived estrogen biosynthesized from adipose tissue *via* the steroid hormone metabolic pathway within an overweight background in our patient. The ectopic endometriotic lesions in the fallopian tube were obstructed by the blocked end of the fimbriae to be disseminated into the pelvic cavity, then they invaded the tubal myometrium, and were ultimately stimulated by estrogen to promote tumorigenesis. The endometrium was also similarly and persistently induced by estrogen to ultimately initialize carcinogenesis.

Second, according to the algorithms of Scully *et al*[11], the fallopian tube endometrioid adenocarcinoma with superficial myometrial infiltration was surrounded by atypical hyperplasia upon an endometriotic background, while the EEA showed less than 50% myometrial invasion without lymphovascular invasion or distant metastasis. Third, tumor biomarkers such as CA125, CA153, and CA199 were unremarkable, while only HE4 was slightly elevated, which was inconsistent with endometrial cancer accompanied by fallopian tube metastasis. These pathological and clinical characteristics supported both fallopian tube and endometrial cancer occurring independently. We consequently proposed that the tumorigenesis in both the fallopian tube and endometrium was contemporaneous.

CONCLUSION

In clinical practice, making a differential diagnosis of concurrent primary cancer of the fallopian tube and endometrium from fallopian metastasis of endometrial cancer, which involves post-adjuvant treatment decisions and oncologic outcomes, is challenging. Using Scully algorithms, we might be able to make a proper differential diagnosis when confronted with concurrent cancers derived from multiple sites of the female genital tract. In this case report, we demonstrated a concurrent endometriosis-associated endometrioid cancer of the fallopian tube and primary endometrial cancer in a premenopausal woman. Fortunately, the pathological identification of malignant transformation in the fallopian endometriosis lesion led to distinct differentiation from primary endometrial cancer dissemination.

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FOOTNOTES

Author contributions: Feng JY contributed to primary manuscript writing, conceptualization, and data collection; Jiang QP contributed to pathologic review; He H contributed to manuscript editing, conceptualization, and supervision; all authors have read and approved the final manuscript.

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