A case of squamous cell carcinoma arising from endometriosis of the ovary

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Summary

Ovarian endometriosis sometimes develops into ovarian cancer, especially clear cell adenocarcinoma and endometrioid adenocarcinoma. However, endometriosis rarely develops into squamous cell carcinoma. We present a case of squamous cell carcinoma arising from endometriosis. A 47-year-old Japanese woman was given a diagnosis of ovarian squamous cell carcinoma arising from endometriosis. She was treated with combination chemotherapy consisting of paclitaxel and carboplatin once every three weeks. Four months after the initial chemotherapy, multiple liver tumors appeared, and her treatment was changed to palliative therapy. Based on this case, in which ovarian squamous cell carcinoma arose from endometriosis, endometriosis should be followed-up strictly.

Key words: Squamous cell carcinoma; Ovarian cancer; Endometriosis.

Introduction

Malignant transformation of endometriosis is sometimes observed in ovarian cancer, especially to clear cell adenocarcinoma and endometrioid adenocarcinoma [1, 2]. Ovarian squamous cell carcinoma is usually associated with either a benign cystic teratoma or a Brenner tumor [3]. We present an extremely rare case of ovarian squamous cell carcinoma arising from endometriosis.

Case Report

A 40-year-old unmarried woman with no previous history of disease underwent a Papanicolau test in 1999 and a cystic mass in her left adnexa was found. In 2003, at age 44, she underwent laparoscopic cystectomy of a left ovarian endometrial cyst with a postoperative pathological diagnosis of endometriosis. She had been administered GnRH analogue six times before this operation. We followed her up every six months, however, the left ovarian cyst recurred two years after the first operation. In 2006, at age 47, she underwent a re-operation. She had a fever of 39°C and complained of melena three months before the second operation. Magnetic resonance imaging (MRI) scans suggested that the left ovarian 100 × 90 mm mass was infected. Colonofiberoscopy revealed stenosis of the sigmoid colon with inflammation but no tumor. We believed this stenosis had been caused by endometriosis. Her infection was treated with antibiotics, and she recovered. Thereafter we administered GnRH analogue to her four times before the second operation.

During laparoscopic surgery, a left ovarian mass 100 × 60 mm with marked adhesion to the sigmoid colon was found, causing the frozen pelvis. The mass ruptured during the cystectomy and we found that the mass had an internal solid component. Intraoperative frozen-section revealed poorly differentiated transitional cell carcinoma. Therefore, we converted from laparoscopic surgery to a laparotomy, with total hysterectomy, bilateral salpingo-oophorectomy, pelvic and paraaortic lymphadenectomies, omentectomy, and sigmoidectomy. There was no residual tumor.

The postoperative, pathological diagnosis revealed that most of the tumor was squamous cell carcinoma (Figure 1) with the remained being transitional cell carcinoma. The International Federation of Gynecology and Obstetrics classification (FIGO) was Stage II C. Blood samples obtained just before the second operation showed her SCC serum levels to be 15 ng/ml. She was then treated with adjuvant combination chemotherapy consisting of paclitaxel (175 mg/m^2 day 1) and carboplatin (AUC 5, on day 1) every three weeks for a total of six courses. Eight months after the operation, her SCC serum levels were elevated and her abdominal MRI scans showed a 64 × 60 mm pelvic mass that was located in contact with the bladder, which we considered to be a relapse. Second-line chemotherapy was given, irinotecan (60 mg/m^2, on days 1, 8, and 15) and cisplatin (60 mg/m^2, on day 1). After two courses, the pelvic mass was enlarged, so the patient was treated with radiation therapy – whole pelvic irradiation totaling 60 Gy. After irradiation, computed tomography (CT) scans demonstrated multiple liver masses, at which time, the patient was changed to palliative therapy.

Discussion

Endometriosis is a common disease, which sometimes develops into ovarian cancer. Recent reports have shown that 0.5-1% of endometriosis causes ovarian cancer. We applied the Sampson and Scott criteria regarding the diagnosis of ovarian cancer developing from endometriosis in this case [4]. These criteria are: (1) Endometriosis and carcinoma occur in the same ovary and the relationship between the benign tissue of endometriosis and the malignant tumor tissue is comparable to that observed in cases of carcinomas developing in the orthotopic endometrium of the uterine corpus. (2) The malignant neoplasm must grow from the endometriosis, not into it. (3) The presence of endometrial stroma, old hemorrhage, or hemosiderine deposits supports the diagnosis of endometriosis. (4) Microscopically, it is possible to demonstrate transition of non-neoplastic into neoplastic epithelium. Since these criteria were fulfilled in this case, we believed that this carcinoma had developed from endometriosis (Figure 1).

Revised manuscript accepted for publication February 3, 2011

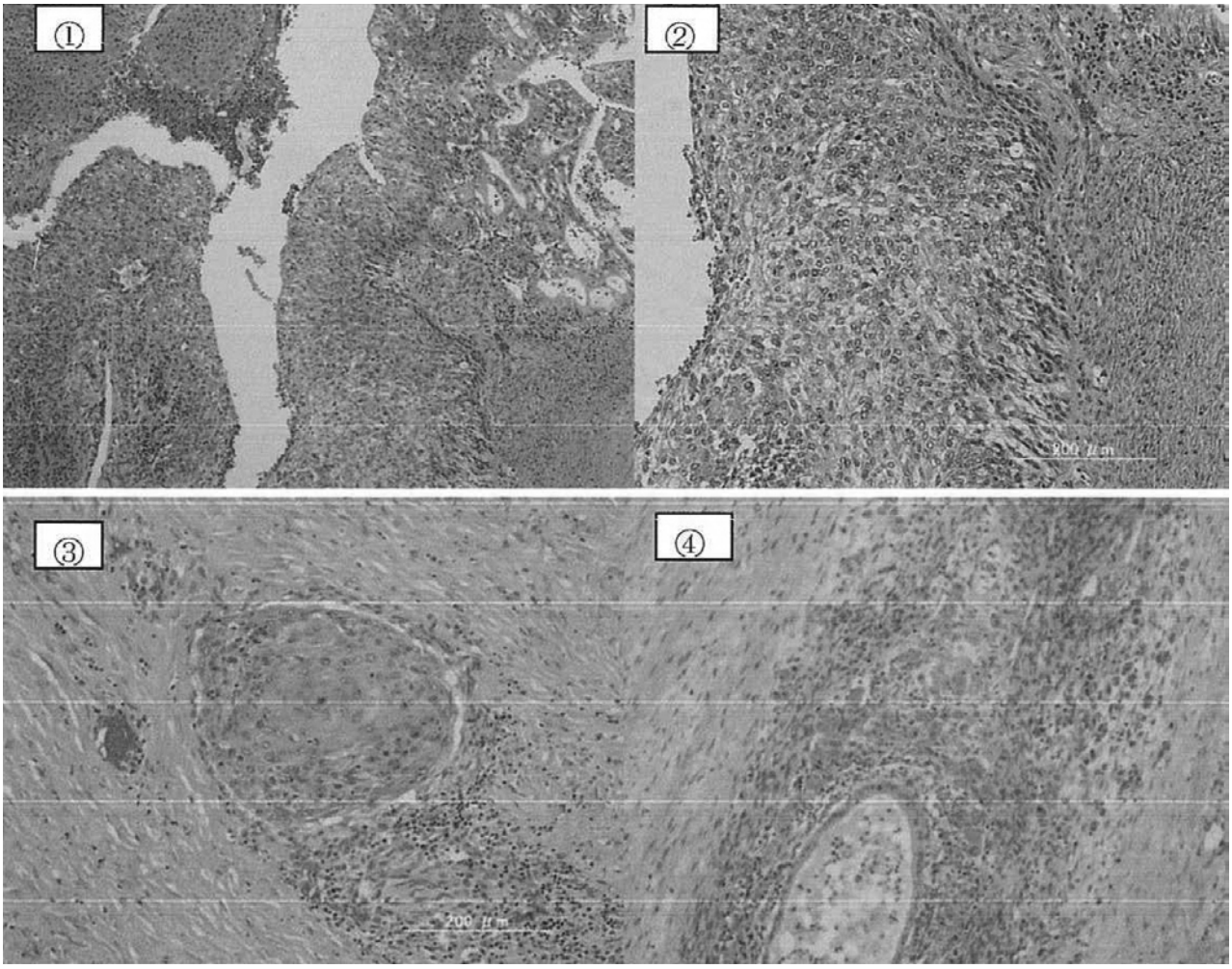

Figure 1. — Hematoxylin and eosin staining in ovarian squamous cell carcinoma associated with endometriosis.
① The continuity from endometriosis to squamous cell carcinoma.
② Focus of continuity from endometriosis to squamous cell carcinoma.
③ Keratinizing squamous cell carcinoma infiltrating the fibrous wall.
④ Ovarian endometriosis.

Endometriosis is usually associated with clear cell adenocarcinoma or endometrioid adenocarcinoma, and ovarian squamous cell carcinoma usually develops from either a benign cystic teratoma or a Brenner tumor [1-3]. In this case, since most of the tumor consisted of squamous cell carcinoma consistent with endometriosis, we diagnosed ovarian squamous cell carcinoma arising from endometriosis.

A search of Pubmed revealed that 16 ovarian squamous cell carcinoma cases have been reported [3, 5-12] (Table 1). The median age of the patients was 49 (range 29 to 86), and the median size of the tumor diameter was 10.8 cm. All cases were resected and adjuvant chemotherapy was given in ten cases, radiation therapy in five cases, and both in four cases. The overall survival was only four months in these cases, implying no response to treatment and extremely poor prognosis.

We could not make a correct diagnosis of ovarian cancer in this case before the second operation. Kobayashi *et al*. [13]. previously showed the risk factors of malignant change from endometriosis to be age greater than 45 years old, a postmenopausal state, and cystic diameter above 100 mm. Furthermore, the risk signs of malignant change on ultrasound examination have also been reported as tumor size increasing in a short period, an intracystic component, and the disappearance of the strong echogenic pattern with increasing diffuse hypoechoic areas. Tumor marker serum level elevation, especially CA-125, is also a risk factor of malignant change.

Preoperative adjuvant treatment, such as GnRH analogue, was performed in this case, but the ovarian tumor was increased. Ovarian carcinogenesis from endometriosis may be reactive to GnRH analogue. Kobayashi *et al*. [13] reported that an ovarian endometrial cyst was decreased at the beginning of GnRH analogue, but although administration was continuous, tumor size was

Table 1. — *Clinical features of 16 previously reported cases and the present case.*

Case	Age	Diameter (cm)	Stage	Treatment	Overall suvival
1	61	unknown	II	RSO	DOD at 6 months
2	62	10	II	ATH, BSO, TR Chemo	DOD at 2 months
3	36	15	Ic	RSO, Rad, Chemo	DOD at 3 months
4	86	unknown	III	TR	DOD at 3 months
5	45	13	III	TR, Rad, Chemo	DOD at 5 months
6	38	13	IIb	LSO, Chemo	DOD at 11 months
7	66	10.5	Ib	ATH, BSO	Alive at 8 months
8	41	unknown	IIb	ATH, BSO, TR	(–)
9	41	7.5	IIb	ATH, BSO, TR,	DOD at 8 months
10	59	12	IIc	BSO, Rad, Chemo	DOD at 6 months
11	70	8	IIIc	ATH, BSO, Rad, Chemo	DOD at 6 months
12	29	8	IV	ATH, BSO, Rad	DOD at 2 months
13	31	10	IV	ATH, BSO, TR, Chemo	Alive at 2 years
14	38	15	IV	ATH, BSO	DOD at 3 months
15	44	6.5	Ia	ATH, BSO, Chemo	Alive at 6 months
16	46	13	IV	ATH, BSO, Sigmoidectomy, Chemo	DOD at 2 months

RSO: right salpingo-oophorectomy; ATH: abdominal total hysterectomy; BSO: bilateral salpingo-oophorectomy; TR: tumor reduction; Chemo: chemotherapy; Rad: radiation therapy; OP: total hysterectomy, bilateral salpingo-oophorectomy, pelvic and para-aortic lymphadenectomy, omentectomy, and sigmoidectomy.

enlarged which increased the risk of developing ovarian cancer.

Squamous cell carcinoma of the ovary associated with endometriosis has an extremely poor prognosis. The average overall survival was only four months in past cases because of minimal response to therapy. In the literature, a few cases demonstrated good response to the therapy that used cisplatin or carboplatin with paclitaxel after radical surgery. However, there is no evidence that these improve overall survival in patients. Ovarian endometriosis should be recognized as a pre-cancerous lesion for which more careful further investigation has to be performed.

Acknowledgements

The authors would like to thank the Language Consultant at the Department of International Medical Communications, Tokyo Medical University, Professor J.P. Barron, for his editorial assistance.

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