Ovarian endometriosis associated with carcinoma and sarcoma: case report

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Summary

Endometriosis is a common clinical disorder that shares certain characteristics, metastasis and recurrence, with malignant neoplasms. Most malignant ovarian tumors arising from endometriosis are clear cell carcinoma or endometrioid adenocarcinoma. Few reports exist of sarcoma associated with endometriosis, and even fewer exist of multiple types of malignancies occurring simultaneously. Here, we report the case of a 32-year-old woman who presented with infertility and a pelvic mass. She underwent exploratory laparotomy and bilateral salpingo-oophorectomy. She was then referred to our institution for treatment recommendation. The pathologic findings revealed bilateral endometrioid adenofibroma of low malignant potential, which was associated with endometrioid intraepithelial carcinoma in the left ovary and high-grade sarcoma in the right ovary. Both tumors seemed to have arisen from endometriosis. She was treated with 75 mg/m^2 of doxorubicin and 10 g/m^2 of ifosfamide every three weeks for eight courses. She was later found to have bilateral brain metastases, which were resected and treated by whole-brain irradiation. She was again treated with doxorubicin and ifosfamide. The optimal treatment for endometriosis-associated ovarian cancer depends on the type of malignancy; simultaneously occurring multiple tumor types should be treated individually.

Key words: Ovary, endometriosis; Carcinoma; Sarcoma.

Introduction

Endometriosis is a common clinical disorder, found in 10%-15% of women [1]. Although endometriosis is benign, malignant ovarian tumors arising from endometriosis have been found in approximately 1.0%-1.5% [2].

In 1925, Sampson [3] reported the first case series of cancer arising in endometriosis and proposed three criteria for its diagnosis: 1) clear evidence of endometriosis found close to the tumor, 2) histopathologic appearance consistent with that of endometriosis (resembling endometrial stroma surrounding characteristic glands), and 3) no other primary tumor site found. In 1953, Scott [4] added a fourth criterion: microscopic continuation, cellular progression from one type to another, between benign endometrioid tissue and malignant tumor tissue. Most reported cases meet Sampson's criteria, but only few reports meet Scott's criteria [5, 6].

Several case reports and reviews exist of endometriosis-associated ovarian cancer (Tables 1 and 2) [7-19]. However, bilateral endometriosis associated with ovarian cancer of multiple types is rare. Here, we report a case of bilateral endometrioid adenofibroma of low malignant potential, which was associated with endometrioid intraepithelial carcinoma in the left ovary and high-grade sarcoma in the right ovary. The tumors seemed to have arisen from endometriosis.

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Case report

A 32-year-old, gravida 1, para 0 white woman presented in July 2006 with a pelvic mass and a history of infertility at the University of Alabama Hospital. She had a history of pelvic endometriosis for years without other medical diseases. She has been on a careful screening program due to a significant familial history of breast cancer. In July 2006, she underwent a hysterosalpingogram; the procedure was complicated by a pelvic abscess. Exploratory laparotomy of the pelvis revealed 300 cc of ascitic fluid and a 17-cm solid right ovarian mass. On palpation, the surface of the left ovary was abnormal. Both ovarian masses were thought to be malignant; therefore, she underwent bilateral salpingo-oophorectomy, partial omentectomy, pelvic and periaortic lymph node sampling. The uterus was left in place for future fertility. The patient was then referred to The University of Texas M. D. Anderson Cancer Center for treatment recommendation.

A review of the pathologic findings revealed high-grade sarcoma in association with endometrioid adenofibroma of the right ovary; the mass had arisen from an ovarian endometriosis (Figure 1). High-grade sarcoma was also found in one of the three examined right pelvic lymph nodes and one right periaortic lymph node. In the left ovary, we found endometrioid adenofibroma of low malignant potential and endometrioid intraepithelial carcinoma that had arisen from an ovarian endometriosis (Figure 2). These findings met both Sampson's and Scott's criteria. A postoperative computed tomography scan revealed lymphadenopathy of the thoracic inlet and left supraclavicular fossa, a subcentimeter pulmonary nodule in the lingula, right intraperitoneal adenopathy, and a small focus of residual tumor in the right common iliac region.

Fig. 1A

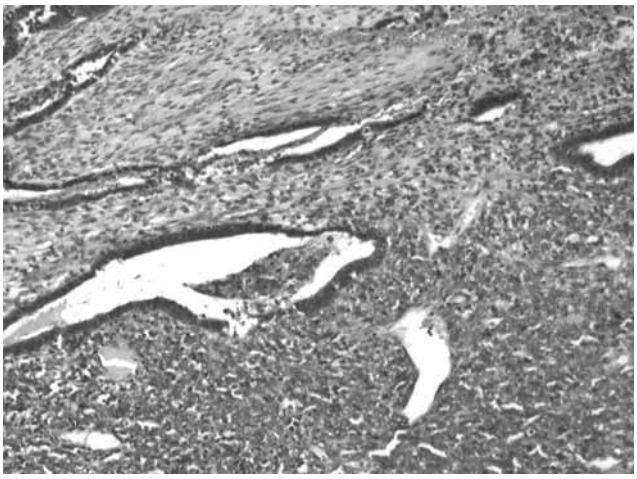

Fig. 1B

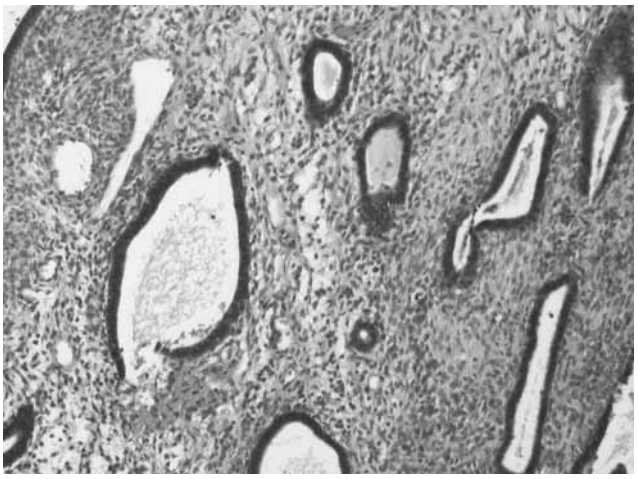

Fig. 2A

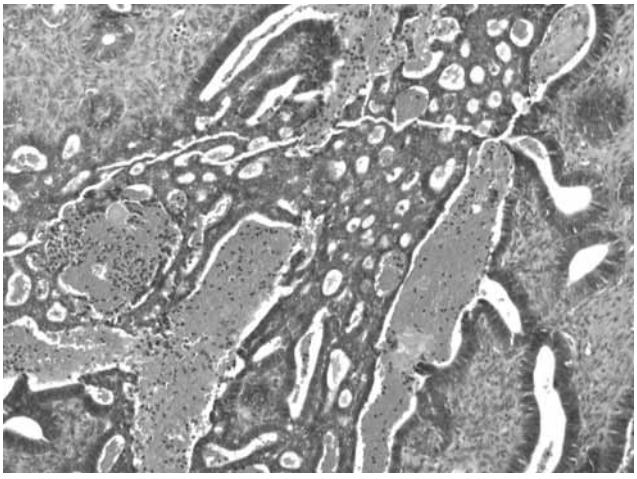

Fig. 2B

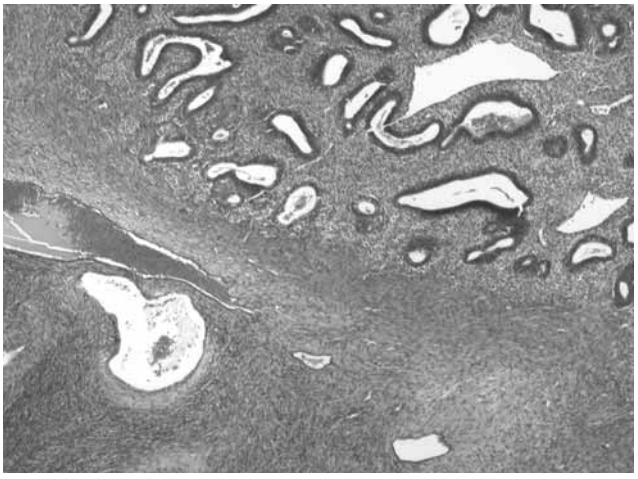

Figure 1. — High-grade sarcoma (lower right) associated with endometrioid adenofibroma (upper left) of the right ovary (A). Endometriosis (B) was found in continuity with the tumor.
Figure 2. — The left ovarian adenofibroma contained glands with a cribriform pattern, consistent with intraepithelial carcinoma (A). Endometriosis involved the surface of the ovary (B) and was in continuity with the adenofibroma.

The patient was treated with systemic chemotherapy, which consisted of 75 mg/m2 of doxorubicin and 10 g/m^2 of ifosfamide every three weeks for eight courses. She was later found to have bilateral brain metastases, which were resected and treated by whole-brain irradiation in April 2007. She was again treated with doxorubicin and ifosfamide. Three months after surgery, she was still on treatment.

Discussion

Endometriosis has been found in 10-15% of ovarian cancer cases [7]. Malignant transformation of endometrioid lesions occurs in 1.0%-1.5% of cases [2], although this rate may be higher because the tumor could destroy the tissue of origin, eliminating any histopathologic evidence of endometriosis.

The clinical characteristics of endometriosis-associated ovarian cancers are distinct from those of typical ovarian cancer: the patients tend to be younger (45-50 years old) [16, 20-24] and nulliparous [21], like our patient. In addition, at the time of surgery, many endometriosis-associated ovarian tumors are Stage I or II and can be completely resected, with no postoperative residual disease [16, 21, 23, 24]. Women with endometriosis-associated ovarian cancer may also have longer disease-free survival durations, and possibly longer overall survival durations than non-endometriosis-associated ovarian cancer [21, 24].

The predominant histologic cell types in endometriosis-associated ovarian cancer are clear cell (8%-70%) and endometrioid carcinoma (9%-43%) (Table 1) [7-17], and most endometrioid tumors are grade 1 or 2 [16, 21, 23, 24]. The patient in our case had endometrioid adenofibroma of low malignant potential in association with endometrioid intraepithelial carcinoma in the left ovary and high-grade sarcoma in the right ovary; both of these appeared to have arisen from endometriosis. Primary ovarian sarcoma is rare, and to our knowledge, no data exists on the relationship between adenofibroma and ovarian sarcoma. Endometrioid stromal sarcoma, on the other hand, is associated with endometriosis (Table 2) [12, 18, 19], and endometriosis-associated malignant mixed mullerian tumor and adenosarcoma have been reported [12].

Table 1. — *Summary of incidence of endometriosis in epithelial ovarian cancer patients*.

Study	Histologic tumor type/*n* of patients with endometriosis/total (%)				
	Endometrioid	Clear cell	Mucinous	Serous	Total
Aure *et al*. 1971 [7]	20/212 (9%)	14/59 (24%)	1/203 (1%)	0/357 (0%)	35/831 (4%)
Kurman *et al*. 1972 [8]	4/37 (11%)	1/12 (8%)	0/33 (0%)	2/118 (2%)	7/200 (4%)
Russel 1979 [9]	20/72 (28%)	16/33 (49%)	3/69 (4%)	7/233 (3%)	46/407 (11%)
Vercellini *et al*. 1993[a] [10]	30/114 (26%)	8/38 (21%)	6/94 (6%)	8/220 (4%)	52/466 (11%)
Toki *et al*. 1996 [11]	16/54 (30%)	22/44 (50%)	3/33 (9%)	9/88 (10%)	50/219 (23%)
Fukunaga *et al*. 1997 [12]	13/31 (42%)	27/50 (54%)	2/35 (6%)	6/63 (10%)	48/179 (27%)
Jimbo *et al*. 1997 [13]	3/13 (23%)	13/32 (41%)	1/35 (3%)	8/92 (9%)	25/172 (15%)
Erzen *et al*. 1998 [14]	2/13 (15%)	1/2 (50%)	0/7 (0%)	0/31 (0%)	3/53 (6%)
Ogawa *et al*. 2000 [15]	3/7 (43%)	30/43 (70%)	0/17 (0%)	4/60 (7%)	37/127 (29%)
Vercellini *et al*. 2000[a] [16]	13/66 (20%)	5/35 (14%)	1/30 (3%)	2/61 (3%)	21/192 (11%)
Takahashi *et al*. 2001 [17]	4/10 (40%)	2/11 (18%)	0/13 (0%)	1/15 (7%)	7/49 (14%)
Total	128/629 (20%)	139/359 (39%)	17/569 (3%)	47/1338 (4%)	331/2895 (11%)

[a]Mixed ovarian cancers were excluded because of insufficient information on the major histologic component.

Table 2. — *Summary of incidence of endometriosis in ovarian sarcoma patients*.

Study	Histologic tumor type/*n* of patients with endometriosis/total (%)			
	Endometrioid stromal sarcoma	Malignant mixed mullerian tumor	Adeno-sarcoma	Total
Young *et al*. 1984 [18]	11/23 (48%)	–	–	11/23 (48%)
Fukunaga *et al*. 1997 [12]	–	1/2 (50%)	1/1 (100%)	2/3 (67%)
Fukunaga *et al*. 1998 [19]	2/3 (67%)	–	–	2/3 (67%)
Total	13/26 (50%)	1/2 (50%)	1/1 (100%)	15/29 (52%)

Heaps *et al*. [25] reviewed 195 previously reported cases of malignant tumors arising in the foci of endometriosis and added their own ten cases in 1990. Of the 205 cases, 183 were carcinomas and 24 were sarcomas; two of these cases involved both types [26, 27]. Our case is similar to the latter two, in that she had two histopathologically different tumors, sarcoma and endometrioid adenofibroma. These findings are suggestive of gradual progression from benign to malignant tumors.

The most important treatment for endometriosis-associated ovarian cancer is surgical resection of the tumor. Postoperative treatment of this disease has varied considerably, however, as yet no concise treatment guidelines exist. Postoperative treatment is especially challenging in patients with multiple histologic tumor types. However, adjuvant chemotherapy has been found to result in longer survival duration and better prognosis than in patients who do not undergo adjuvant chemotherapy [21, 24]. A retrospective study evaluated the use of adjuvant treatments for endometriosis-associated ovarian cancer [21, 24], including chemotherapy alone, pelvic irradiation alone, chemotherapy and pelvic irradiation combined, and hormonal therapy. The chemotherapy regimens included platinum-based drugs alone and platinum-based drugs with paclitaxel and melphalan. No relationship was found between overall survival and postoperative treatment modality (chemotherapy vs radiation) on univariate analysis. However, significant predictors of overall survival were identified: the stage, grade, and histologic type of the tumor and the type of postoperative chemotherapy. Women treated with platinum alone had poorer overall survival rates than did those treated with platinum-based combined chemotherapy. In the multivariate analysis, however, only stage remained an independent significant predictor of the rate of overall survival [21, 24].

Sarcoma is more difficult to treat. Young *et al*. [18] reported the largest series of ovarian endometrioid stromal sarcoma associated with endometriosis. Low-grade sarcoma was associated with longer survival, with no adjuvant treatment, in four patients. Two patients treated with chemotherapy and progesterone were alive after one year and five years. Pelvic irradiation was effective in four patients, leading to survival durations of one, two, four and ten years. Only two of the 19 patients with low-grade tumor, compared to three of four patients with high-grade tumor, died of their disease. Two patients with high-grade disease, who had been treated postoperatively with chemotherapy, died of their disease after two and three years. Another patient with high-grade disease was treated with chemotherapy and radiation; she died five months later. Only one patient with high-grade disease – who was treated with radiation and methotrexate – was still alive after five years [18].

Marchevsky and Kaneko [27] reported a case of bilateral endometriosis associated with carcinosarcoma of the right ovary and endometrioid carcinoma of the left ovary. The patient was successfully postoperatively treated with doxorubicin and ifosfamide. Cooper [26] reported a case of mixed mesodermal tumor and clear cell carcinoma arising in ovarian endometriosis but did not provide treatment information. The patient in our report received eight courses of doxorubicin and ifosfamide but subsequently experienced brain metastasis. She underwent surgical resection, whole-brain irradiation, and salvage chemotherapy. Three months after surgery, she was still on treatment.

The optimal treatment for endometriosis-associated ovarian cancer depends on the type of malignancy; simultaneously occurring multiple tumor types should be treated individually.

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