Serous Adenocarcinofibroma of the Ovary
— Report of Two Cases and Review of the Literature —

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Summary: We investigated the clinical and histologic characteristics of patients with ovarian serous adenocarcinofibroma. Because the tumors in both cases contained fibroma components; they were hard and clinically indistinguishable from uterine myoma, even by computed tomography. Both patients experienced relapses associated with tumors that originated outside the abdominal cavity (the subcutaneous abdominal wall in case 1, and the inguinal lymph nodes in case 2). The serum level of CA125 was normal or only moderately elevated at the first onset and relapse. The present cases suggest that the diagnostic features and clinical course differ between ovarian serous adenocarcinoma and serous adenocarcinofibroma.

Key words ovarian cancer, serous adenocarcinofibroma

INTRODUCTION

Adenocarcinofibroma of the ovary is rare. Since the first cases were described by Morris and Scully [1] in 1958, only 42 subsequent cases have been described in the literature [2-5]. Although the morphological characteristics of these tumors have been extensively examined, the clinical characteristics are not fully understood. Although adenocarcinofibroma is histologically classified as an epithelial ovarian carcinoma [6], some investigators [7,8] have proposed reclassifying this condition as a separate disease entity. We investigated the histologic and clinical characteristics of 2 patients with serous adenocarcinofibroma of the ovary.

CASE REPORT

Case 1

A 62-year-old Japanese woman visited a private hospital because of irregular vaginal bleeding in September 1991. Uterine leiomyoma was diagnosed based on the clinical findings, and a supravaginal hysterectomy and bilateral salpingo-oophorectomy were performed.

A goose-egg sized myoma and a larger right ovarian tumor (7×7×6 cm) were detected at laparotomy. No other abnormalities were observed in the abdominal cavity. Examination of a section of the tumor showed primarily a solid structure that contained several small cystic lesions. Microscopy revealed serous adenocarcinomatous components invading the prominent stroma. Fibrous cells proliferated sporadically, forming nests of fibroblasts, in the stroma which is characteristic of serous adenocarcinofibroma (Fig. 1). The patient was referred to Kurume University Hospital for further evaluation. Because staging of the tumor at the time of the first surgery was unsatisfactory, we recommended staging surgery and adjuvant treatment, but this was refused by the patient. A solitary subcutaneous tumor was observed beneath the navel in July 1992 (Fig. 2). Pathological examination of a tumor specimen confirmed a recurrence of the adenocarcinofibroma. The disease progressed rapidly over the next 3 months, and the patient underwent cytoreductive surgery due to peritonitis carcinomatosa in October 1992. The

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CASE 1

Subserosal uterine myoma was diagnosed based on clinical examination in a 50-year-old post menopausal Japanese woman with vaginal bleeding. The serum level of CA125 was moderately elevated 200 U/ml. A malignant ovarian tumor was identified at laparotomy in July 1991, and the patient underwent staging surgery. The tumor measured 10×7×8 cm and was a dark yellow color. No metastases were macroscopically observed in the abdominal cavity. The sectioned surface of tumor was almost solid and a pale yellowish-white and included a cystic lesion containing a pale brown liquid, suggesting hydropic degeneration of the fibroma (Fig. 3). Histological examination showed serous cystadenocarcinoma invading the fibrous stroma which contained nests of proliferating spindle cells. These findings are characteristics of adenocarcinofibroma (Fig. 4). Occasional psammoma bodies were observed in the carcinoma components. Although the tumor did not extended into the peritoneal cavity, metastases of the bilateral pelvic lymph nodes, which were normal in size, were detected. Histological exami-
nation of the lymph nodes also revealed serous adenocarcinofibroma. The postoperative clinical stage was PT aN1M0. After surgery, the patient received 4 courses of combination therapy consisting of 350 mg/sq of cyclophosphamide, 30 mg/sq of adriamycin, and 50 mg/sq of cisplatin every 4 weeks. The serum level of CA125 did not decrease during therapy. She subsequently received 2 courses of therapy with carboplatin (350 mg/sq on day 1) plus cisplatin (50 mg/sq on day 3) every 4 weeks. But the serum level of CA125 failed to decrease. She was then treated with 5 courses of therapy with cisplatin (50 mg/sq on day 1) plus CPT11 (50 mg/sq on day 1, 8 and 15) every 4 weeks. The serum level of CA125 normalized after 3 courses of this therapy and the patient was discharged from the hospital. No second-look operation was performed.

Although no abnormal findings were detected by computed tomography, the serum level of CA125 began to increase in July 1993. She underwent exploratory laparotomy in November 1993. Although no evidence of recurrence was observed in the abdominal cavity, she received 2 courses of consolidation chemotherapy with carboplatin (300 mg/sq intraperitoneal transfusion) plus etoposide (25 mg/every day, per os) every 4 weeks. Despite this treatment, she experienced a recurrence of the cancer on the right side of inguinal lymph node (Fig. 5) in May 1994. After 3 courses of CPT−11+ cisplatin combination chemotherapy, she achieved a partial response. Until May 1996, she has continued to receive this therapy at 4 months interval. However, the tumor gradually progressed and she died in August 1998.

DISCUSSION

Surface epithelial-stormal tumors of the ovary originate from the surface epithelium and the stroma, which is beneath the surface epithelium. Most of these tumors are epithelium-oriented. However, some are fibroma-tissue-oriented and are classified as fibromas. Adenocarcinofibromas are also known as malignant adenofibromas, and an adenocarcinoma that arises from an adenofibroma is defined as an adenocarcinoma occurring in the form of cytologically malignant epithelial cells that invade the stroma. Adenocarcinofibromas are rare ovarian tumors with only 42 cases previously reported. Timonen and Purolar [9], however, have suggested that the incidence of adenocarcinofibroma is higher than previously thought. Randrianjafisamindrakotroka et al. [5] diagnosed 845 cases of ovarian epithelial tumors during a 10-year periods, and 118 of these cases were either adenofibroma or cystadenofibroma, and 5 were carcinoma. The reported incidence of these types of tumors varies probably because there is no definitive diagnostic criteria for adenocarcinofibroma.

On the other hand, adenofibromatous changes represent a unique stormal reaction of the ovary to invading neoplastic cells [10], usually found in serous type tumors [7,8,11]. Although the histologic features of ovarian tumors with a fibroma pattern have been described [12], clinical course of these tumors has not been extensively investigated. The present findings suggest that the diagnostic characteristics and clinical courses of adenocarcinofibroma differ from those of serous adenocarcinoma.

It was difficult to distinguish the present cases of adenocarcinofibroma from uterine myoma preoperatively because the tumors had hard surfaces due to their rich fiber content and because the computed tomography and ultrasonography showed findings similar to those associated with uterine myoma or its transformation. Moreover, the serum level of CA125 which is the most reliable marker of malignant ovarian tumors [13] was normal or only moderately elevated in the present cases, although the tumors were serous adenocarcinoma. The serum level of CA125 was normal at the first relapse in Case 1, and did not increase until the patient experienced second relapse. In Case 2, the preoperative serum level of CA125 was only 200 U/ml. It is possible that the tumor cells produced only a small amount of CA125 or that the fibroma tissue surrounding the tumor cells prevented the cancer antigen from entering the
vascular bed. Both patients in the present study developed relapses, and one died. Metastases developed in the fascia or the inguinal lymph node, whereas generally serous adenocarcinoma recurs such as in the abdominal cavity or the retroperitoneal cavity.

Previous studies have suggested that adenocarcinofibroma is less malignant and does not spread or become implanted in most cases [2]. According to Kao et al. [11] cystadenofibroma with epithelial atypia has similar epithelium to that of low potential malignancy (LPM) of cystadenoma, and the former has 100% of the survival rate, whereas 5 and 15-year survival rates of the patients with LPM of cystadenoma are 95% and 85%, respectively. Because the overall number of adenocarcinofibroma cases is limited and furthermore the most reported cases contain little or no follow-up data, long-term follow-up studies of patients with adenocarcinofibroma are needed to clarify the clinical and histologic characteristics of this type of tumor. Randrianjafisamindrakotroka et al. [5] reported that 3 of 5 patients with adenocarcinofibroma died, 2 of whom experienced tumor recurred, 1 was lost to follow up, and the other has survived for 9 years. The potential malignancy of the ovarian adenofibroma, therefore, is unneglectable and needs to be precisely examined.

The most common presenting symptom of a patient with cystadenofibroma is abdominal pain [14]. Another common symptom is abnormal vaginal bleeding [9,11], which may be related to a possible endocrine effect of the tumors leading to the abnormal proliferation of the endometrium [9]. Both patients in the present study had abnormal vaginal bleeding. Kurman et al. [15] detected testosterone and estradiol by immunohistochemistry in ovarian primitive spindle cells. The ovarian stroma may produce such sex steroids.

Ovarian serous tumors with adenofibroma or an adenofibroma pattern are variants of serous adenoma of the ovary [16,17]. The present clinical and histologic finding suggest that these neoplasms constitute a separate disease entity.

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REFERENCES