She had a strong family history of breast and ovarian cancers and genetic study suggested a lifetime risk of breast cancer of 80–90 per cent. She opted for total abdominal hysterectomy and bilateral salpingo-oophrectomy, which was performed 8 weeks after the first operation. The histopathology report revealed a reactive mesothelial cells in the peritoneal washing and a primary adenocarcinoma of the left fallopian tube stump which remained after surgery for the ectopic. After the surgery, she had adjuvant chemotherapy with single agent carboplatin.

A year later, clinical and imaging (CT scan) examinations showed no signs of recurrence.

Discussion

The prospect of cure is dependent upon the stage at which the disease is discovered. The place of omentectomy is not yet established. Postoperative chemotherapy will be required for the majority of cases. Postoperative radio-therapy has been tried, but the relative worth remains controversial. The overall 5-year survival is around 35 per cent. It is in the region of 70 per cent for stage 1 disease.

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Correspondence to: Dr Jane Preston, Department of Obstetrics & Gynaecology, James Paget Hospital, Lowestoft Road, Garleston, Great Yarmouth, Norfolk NR31 6LA, UK.

Two case reports of ovarian cancer after long-term tamoxifen treatment for breast cancer

N. OHARA[1] and A. KOBAYASHI[2]

Departments of [1]Obstetrics and Gynecology, Kohnan Hospital, Kobe, Japan and [2]Obstetrics and Gynecology, Kaisei Hospital, Kobe, Japan

Case report

Case 1

A 68-year-old postmenopausal woman underwent a standard radical mastectomy for stage II infiltrating ductal breast cancer in 1982. Tamoxifen (20 mg/day) had been administered as adjuvant therapy until 1994, when she presented with abdominal fullness. Magnetic resonance imaging revealed a 10-cm left cystic adnexal mass with a mural nodule showing intermediate to high signal intensities both on the T1- and T2-weighed images. Laparotomy confirmed a left ovarian tumour without evidence of peritoneal spread. A total abdominal hysterectomy and the bilateral salpingo-oophorectomy were performed. Histology revealed a clear cell carcinoma of the left ovary. She received chemotherapy with mitomycin-C and cyclophosphamide, followed by maintenance chemotherapy with daily 5-FU administration. Massive ascites developed 13 months after surgery and she died of the disease.

Case 2

A 56-year-old postmenopausal woman underwent a standard radical mastectomy for stage II infiltrating ductal breast cancer in 1983. She had taken tamoxifen (20 mg/day) for 9 years. She was referred for examination of an adnexal mass in 1992. A computed tomographic scan revealed a right adnexal mass with a mural nodule and ascites. Laparotomy revealed a right ovarian tumour, ascites with malignant cytology, extensive peritoneal dissemination and omental nodules. A total abdominal hysterectomy, bilateral salpingo-oophorectomy and omentectomy were performed. Microscopic examination showed an undifferentiated carcinoma of the right ovary. She received intraperitoneal administration of cisplatin, followed by systemic chemotherapy with cisplatin, cyclophosphamide and adriamycin, and then additional intraperitoneal administration of etoposide. Liver metastasis developed 18 months after surgery and she died of the disease.

Discussion

Tamoxifen is a non-steroidal anti-oestrogen that is used widely as adjuvant therapy for postmenopausal breast cancer patients. Recently, concerns have been focused on the possible relationship between tamoxifen use and the development of a second primary ovarian cancer. Previous reports have described the occurrence of ovarian cancers during tamoxifen therapy, including clear cell carcinoma (Jennings *et al.*, 1999), endometrioid carcinoma either associated with endometriosis (McCluggage *et al.*, 2000) or not associated with endometriosis (Kuo *et al.*, 1997), papillary serous carcinoma (Seoud *et al.*, 1999), granulosa cell tumour (Gherman *et al.*, 1994) and androgen-producing ovarian tumour (Surbek *et al.*, 1998). Several authors suggested the mechanism by which tamoxifen may induce ovarian cancer to be the direct stimulation of ovarian epithelial tissue (Kuo *et al.*, 1997), oestrogenic effect on extrauterine endometrial tissue (Jennings *et al.*, 1999; McCluggage *et al.*, 2000) and abnormal accumulation of tamoxifen's oestrogenic metabolites with tamoxifen-induced liver dysfunction (Gherman *et al.*, 1994). Cohen *et al.* (1996) have described that women with breast cancer are prone to develop ovarian cancer while on tamoxifen therapy, and that tamoxifen may stimulate the growth of ovarian tumours in postmenopausal breast cancer patients.

However, published cases are limited and they have not established a cause-and-effect relationship. Two authors only described a need for vigilance for the development of ovarian cancer in breast cancer patients treated with tamoxifen (Jennings *et al.*, 1999; Seoud *et al.*, 1999). On the other hand, McGonigle *et al.* (1999) reported that tamoxifen-treated patients were less likely to have ovarian cancer on the basis of ovarian pathology in a series of 152 breast cancer patients undergoing oophorectomy, suggesting no association between tamoxifen exposure and an increase in ovarian cancer. The molecular mechanism of the action of tamoxifen on ovarian epithelium remains unknown.

The known influence of cancer genes BRCA1 and BRCA2 on the occurrence of both breast cancer and ovarian cancer makes assessment of a cause-and-effect relationship between tamoxifen use and ovarian cancer specifically difficult. In conclusion, it seems probable that there exists no convincing evidence to support the view that tamoxifen is a causal factor of ovarian carcinogenesis.

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Correspondence to: Noriyuki Ohara, Department of Obstetrics and Gynecology, Kohnan Hospital, 5–16, 1-Chome Kamokogahara, Higashinada-Ku, Kobe, Hyogo Prefecture, 658–0064, Japan. Tel: 078 851 2161; Fax: 078 821 0962.

Chemotherapy for ovarian adult granulosa cell tumour with synchronous endometrial adenocarcinoma

N. OHARA,[1] K. TERAMOTO[1] and S. MURAO[2]
Department of [1]Obstetrics and Gynecology and [2]Pathology, Kohnan Hospital, Kobe, Japan

Case report

A 67-year-old woman presented with abdominal fullness in 1994. Ultrasonographic examination revealed an enlarged uterus and a hypoechoic monocystic mass in the right adnexa, measuring 9·3 × 7·5 cm in diameter. The cytology of the endometrium showed adenocarcinoma cells, although that of the cervix was normal with low oestrogen index (KI). Computed tomographic scan demonstrated the uterus with a thickened endometrium and a cystic mass with an irregularly thickened wall. No ascites or pelvic lymphadenopathy was noted. Serum CEA was within normal limits, whereas serum CA19–9 (43 U/ml) and CA125 (58 U/ml) were slightly elevated.

Based on the clinical diagnosis of stage Ia endometrial carcinoma and a right ovarian tumour, a total hysterectomy and bilateral salpingo-oophorectomy were carried out. The cytology of peritoneal washings revealed no atypical cells. Pathological examination revealed an adult granulosa cell tumour (GCT) of the right ovary and a poorly differentiated adenocarcinoma of the endometrium. In the GCT, fairly uniform and round neoplastic cells with hyperchromatic nuclei proliferated in an insular growth pattern. Occasional Call–Exner bodies were noted (Fig. 1A). In the endometrial adenocarcinoma, neoplastic cells were infiltrating into the stroma and some tumor cells had vacuolated cytoplasma (Fig. 1B). However, the cervix and the left ovary were free of disease. She received several courses of adjuvant chemotherapy consisting of cisplatin, adriamycin and cyclophosphamide. She has been without evidence of recurrence for 6 years since the initial surgery.

Discussion

A granulosa cell tumour (GCT) is an oestrogen-secreting neoplasm with low malignant potential. The association between hyperoestrogenism caused by GCT, and the development of endometrial hyperplasia and adenocarcinoma has been well documented. Malmström *et al.* (1994) reported that a third of the patients had atypical endometrial cells and five patients had endometrial carcinoma in 54 cases with GCT. In this patient, however, hyperoestrogenic state was less likely because of the low oestrogen index in the cytology of the cervix, suggesting the development of endometrial adenocarcinoma independently of hyperoestrogenism.

The optimal chemotherapy for GCT is probably the BEP regimen (bleomycin, etoposide and cisplatin). In contrast, complete and partial responses have been attained with combination of cisplatin, doxorubicin and/or cyclophosphamide in the patients with GCT (Jacobs *et al.*, 1982; Camlibel and Caputo, 1983). Therefore, we conducted the CAP regimen, considering the efficacy for both GCT and endometrial adenocarcinoma, and the effect of this regimen was confirmed on the basis of 6-year disease-free survival. This patient illustrates that the CAP regimen may be a candidate as the first-line chemotherapy when the patient with GCT has associated endometrial adenocarcinoma.

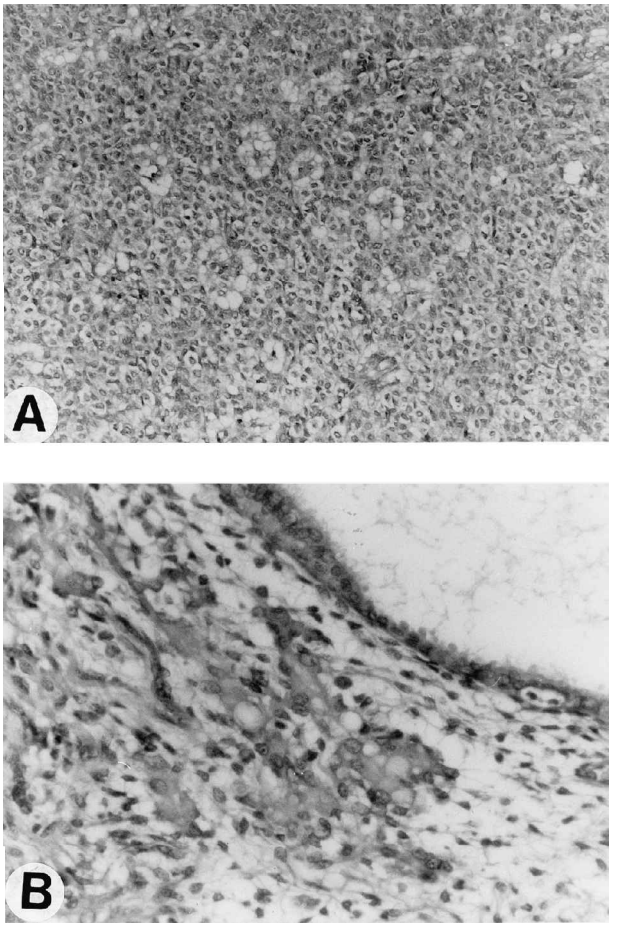

Figure 1. Pathological findings of adult granulosa cell tumour and endometrial adenocarcinoma. (A) Diffuse sheet of adult granulosa cell tumour cells, showing several Call-Exner bodies (H&E stain, × 200). (B) Poorly differentiated endometrial adenocarcinoma cells infiltrating into stroma, disclosing vacuolated cytoplasma in some tumour cells (H&E stain, × 400).