Synchronous squamous cell carcinoma of the endometrium and endometrioid adenocarcinoma of the ovary

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Summary

Background: Synchronous primary endometrial and ovarian cancers are relatively uncommon in general population. The etiology and pathogenesis of this phenomenon remains unclear. The authors' aim was to present a case of synchronous squamous cell carcinoma of the endometrium and endometrioid adenocarcinoma of the ovary and review current literature. *Case:* The patient, a 64-year-old, nulliparous postmenopausal Greek woman presented with a complaint of abdominal pain and abnormal uterine bleeding. Preoperative computer tomography (CT) of the abdomen and pelvis, and abdominal ultrasound (U/S) revealed an intra-abdominal three cm mass with solid components between the left ovary and small bowel. The patient underwent total abdominal hysterectomy with bilateral salpingo-oophorectomy (TAH+BS), total omentectomy, pelvic and para-aortic lymph node dissection, and removal of the implant at the serosa of small bowel. Histopathology revealed Stage IA endometrial cancer squamous type and Stage IIIC ovarian cancer of endometrioid-type. Postoperatively the patient underwent adjuvant chemotherapy and radiotherapy. Follow-up of 22 months after initial surgery revealed no evidence of recurrence. *Conclusion:* The reason for better median overall survival of patients with synchronous primary endometrial and ovarian cancers is not intuitively obvious. Perhaps favourable clinical outcome may be related with the detection of patients at early stage and low-grade disease with an indolent growth rate.

Key words: Squamous cell carcinoma of the endometrium; Endometrial cancer; Ovarian cancer; Synchronous primary cancers.

Introduction

Synchronous primary cancers are relatively uncommon in general population. About 1-6% of women with gynaecological malignancies have synchronous primary cancers of the female genital tract [1, 2]. Synchronous primary endometrial and ovarian cancers are the most common combination [1, 2].

The etiology and pathogenesis of this phenomenon remains unclear [3, 4]. It has been postulated that embryologically similar tissues, when simultaneously exposed to hormonal influences or to carcinogens, may develop synchronous cancers [3, 4].

The authors' aim was to present a case of synchronous squamous cell carcinoma of the endometrium and endometrioid adenocarcinoma of the ovary and review current literature.

Case Report

The patient, a 64-year-old, nulliparous postmenopausal Greek woman presented at the Second Department of Gynaecology of St. Savvas Anticancer-Oncologic Hospital, with a complaint of abdominal pain and abnormal uterine bleeding. She had surgical history of appendectomy. Her family history revealed no evidence of cancer among the first-degree relatives.

During gynecologic examination there was a palpable pelvic mass. There were no palpable inguinal lymph nodes and the remaining pelvic examination was normal.

Preoperative computer tomography (CT) of the abdomen and pelvis, and abdominal ultrasound (U/S) revealed an intra-abdominal mass three cm with solid components between left ovary and small bowel. CT of the chest, chest X-ray, intravenous pyelography (IVP), colonoscopy, and urethrocystoscopy were normal. Preoperative CA-125 and CA 19-9 were elevated at 561 U/ml and 672 U/ml, respectively.

On exploratory laparotomy, the left ovary was normal in size, with a papillary exophytic appearance. An implant of three cm was found at the serosa of small bowel. Frozen section showed malignancy and the patient underwent TAH+BS, total omentectomy, pelvic and para-aortic lymph node dissection, and removal of the implant at the serosa of small bowel.

Histopathology revealed synchronous primary cancers of the endometrium and left ovary. The endometrial tumor invaded less than one-half of the myometrium (Figure 1). The ovarian tumor invaded and ruptured the capsule of the left ovary, invaded left Fallopian tube, extending to the right ovary, and to the serosa of small bowel (Figure 2). The omentum and 22 totally removed pelvic and para-aortic lymph nodes were negative for metastatic disease. The peritoneal washing smear was negative for malignant cells. The final diagnosis was Stage IA endometrial cancer squamous type and Stage IIIC ovarian cancer of endometrioid, type.

The patient underwent postoperative adjuvant chemotherapy. She received six courses of carboplatinum (AUC 4) and paclitaxel (175 mg/m²). The patient also underwent postoperative adjuvant radiotherapy. She received 5000 cGy of external pelvic radiotherapy and 2000 cGy of intravaginal brachytherapy.

Follow-up at 22 months after initial surgery, with CT of the chest, abdomen, and pelvis, abdominal U/S, chest X-ray, IVP, colonoscopy, and urethrocystoscopy, revealed no evidence of recurrence.

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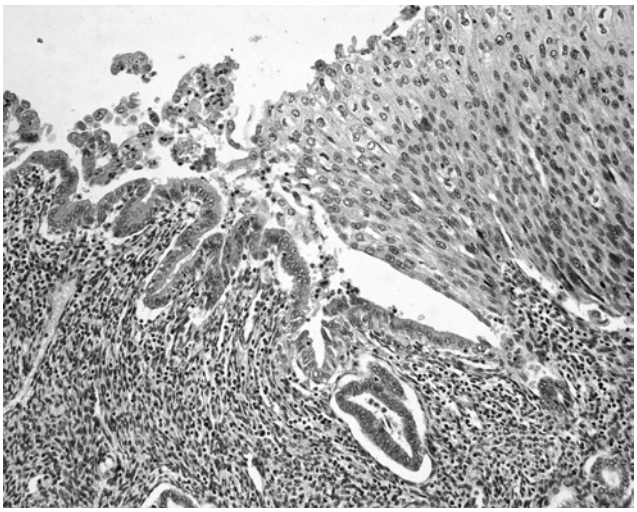
Fig. 1



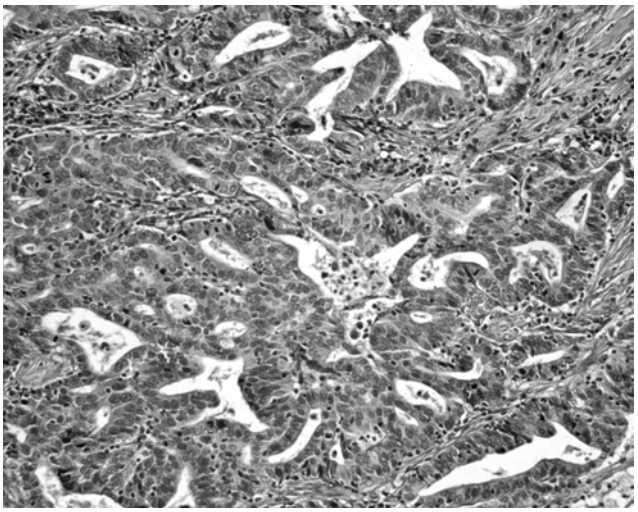


Fig. 2

Figure 1. — Endometrial cancer squamous type: the endometrial tumor invades less than one-half of the myometrium.
Figure 2. — Ovarian cancer of endometrioid-type: the ovarian tumor invades and ruptures the capsule of the left ovary, invades left Fallopian tube, extends to the right ovary, and to the serosa of small bowel.

Discussion

Synchronous primary cancers are relatively uncommon in general population. About 1-6% of women with gynaecological malignancies have synchronous primary cancers of the female genital tract [1, 2]. Synchronous primary endometrial and ovarian cancers are the most common combination [1, 2]. However, primary squamous cell carcinoma of the endometrium is a very rare neoplasm with a prevalence estimated at 0.15 - 0.5% [5, 6]. Only sporadic cases of primary squamous cell carcinoma of the endometrium have been published in the literature. The patient in this study had an extremely rare combination of synchronous squamous cell carcinoma of the endometrium and endometrioid adenocarcinoma of the ovary.

The theory of the "secondary Müllerian system" was proposed to explain the observation of multiple similar cancers in the female genital tract [4, 7]. According to this theory, epithelia of the cervix, uterus, Fallopian tubes, ovaries, and peritoneal surfaces simultaneously respond to a carcinogenic stimulus [4, 7]. Shared hormonal (estrogen) receptors may be responsible for the development of multiple primary malignancies in predisposed tissue [3, 8].

Squamous cell carcinoma of the endometrium are possibly related to bi-directional differentiation of pluripotent endometrial precursor cells, heterotopic cervical tissue or squamous metaplasia (chronic inflammation, pyometra, and previous radiation) [9-12].

It is also possible that the synchronous presence of these cancers is an indicator of an etiologically distinct condition [13]. Perhaps patients have a more fragile genome and prior genetic damage may predispose to synchronous cancers [13-15]. Thus, embryologic, hormonal, or other phenomena may be associated with the development of malignancies arising simultaneously in genital tissues [3, 4, 8-13 15].

Patients with synchronous primary endometrial and ovarian cancers tended to be 10-20 years younger than their counterparts with endometrial or ovarian cancer [16]. The median age at diagnosis was 50 years [17, 18]. They had distinct clinical characteristics including: young age, obesity, premenopausal status, and nulliparity [17]. The most common presenting symptoms and signs were: abnormal uterine bleeding (46%), abdominal/pelvic pain (17%), and abdominal/pelvic mass (13%) [17]. The patient in this study was 64-year-old, postmenopausal, nulliparous, with normal body mass index (BMI), and the main presenting symptoms were abdominal pain and abnormal uterine bleeding.

Synchronous primary endometrial and ovarian cancers may have a similar appearance or may be of different histologic types [16, 18]. The distinction between metastatic and synchronous primary cancers is relatively simple, when they have different histologic types. However, the distinction is relatively difficult when they share the same histologic features [19, 20]. According to the empirical criteria described in detail by Scully *et al*., the patient presented in this study had synchronous primary endometrial and ovarian cancers [20].

Diagnosis in patients with squamous cell carcinoma of the endometrium is especially based on strict pathological criteria [21]. According to the empirical criteria described in detail by Fluhmann, the patient in this study had squamous cell carcinoma of the endometrium [21].

Treatment of choice in early-stage patients with synchronous primary endometrial and ovarian cancers is: TAH+BS, total omentectomy, appendectomy, and pelvic lymph node dissection [18]. Advanced-stage patients, required more aggressive management with postoperative adjuvant chemotherapy and/or radiotherapy [22-24]. According to current treatment strategies, the described patient underwent radical surgery and received postoperative adjuvant chemotherapy and radiotherapy, as she was diagnosed with advanced-stage disease.

Prognostic factors for synchronous primary endometrial and ovarian cancers are: age, stage of ovarian cancer, grade of endometrial cancer, and adjuvant therapy [25]. Patients with synchronous primary endometrial and ovarian cancers of endometrioid-type have a better median overall survival compared with non-endometrioid or mixed histologic subtypes [17]. Also, patients with synchronous primary endometrial and ovarian cancers have overall five-year survival in 85.9% and ten-year survival in 80.3% [18]. The patient in this study had synchronous primary endometrial and ovarian cancer of different histologic type; however, 22 months after initial surgery, she is in good condition with no evidence of relapse.

Conclusion

The reason for better median overall survival of patients with synchronous primary endometrial and ovarian cancers is not intuitively obvious [18]. Perhaps favourable clinical outcome may be related with the detection of patients at early-stage and low-grade disease with an indolent growth rate [14, 15, 23, 26, 27]. Usually endometrial cancer produces earlier symptoms, so synchronous ovarian cancer may be detected at an earlier stage [14, 15, 23, 26, 27].

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