Synchronous primary cancers of the endometrium and ovary: a case report

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Summary

Synchronous primary cancers of the endometrium and ovary are found in 5% of women with endometrial cancer and 10% of women with ovarian cancer. In the present case, a multigravid 46-year-old woman complained of lower abdominal pain and abdominal distension. She did not define abnormal uterine bleeding. Screening ultrasound revealed a papillary containing structure, irregular, cystic 16 x 15 x 10 cm right ovarian mass. Preoperative endometrial biopsy revealed endometrioid adenocarcinoma. Ascites sampling, radical hysterectomy, bilateral salpingo-oophorectomy, pelvic and paraaortic lymphadenectomy, omentectomy, appendectomy and cytologic sampling of the undersurface of the diaphragm were carried out. Intraoperative and histological examinations showed Stage IIIC papillary serous carcinoma and stage IC endometrioid adenocarcinoma. Synchronous genital tract neoplasms constitute a more common clinical problem than would generally be expected.

Key words: Synchronous; Primary cancer; Endometrium; Ovary.

Introduction

The coexistence of carcinoma of the ovary and endometrium is an uncommon event. It occurs in about 10% of patients with ovarian carcinoma and in more than 5% of patients with endometrial carcinoma [1, 2]. Simultaneous involvement of the endometrium and ovary by carcinoma can be classified into three groups: (1) Endometrium cancer with metastasis to the adnexa, (2) ovarian cancer with metastasis to the endometrium, or (3) synchronous primary cancers of the endometrium and ovary [2]. Synchronous primary cancers of the endometrium and ovary are relatively rare, accounting for 0.7% of gynecological malignancies [3]. In many cases recognition of the relationship between two tumors is difficult; however, if the histological types of each cancer are different, this relation can be easily distinguished [2].

Most synchronous primary carcinomas of the uterus and ovary are well differentiated and of the endometrioid cell type (68% of all patients). Twelve percent of all patients have an endometrioid tumor of the endometrium and a component of serous or mucinous carcinoma of the ovary. A few patients have endometrioid carcinoma of the endometrium and clear cell carcinoma of the ovary [1, 5, 6]. The risk factors for women with synchronous primary cancers differ based on the histology of the ovarian tumor. While women with endometrioid/endometrioid histology are young, obese, premenopausal and nulliparous; women with endometrioid/serous histology share similar characteristics with ovarian cancer patients [5].

The etiology of synchronous malignancy is uncertain but it has been postulated that embryologically similar tissues of the female genital tract may develop synchronous neoplasms when simultaneously subjected to carcinogens [3, 7].

This report describes dual primary cancers with two different histologic patterns occurring in both the ovaries and endometrium. Along with this case, the diagnosis, treatment and prognosis of synchronous female genital malignancy is discussed.

Case Report

In March, 2004 a 50-year-old multigravid, thin woman was admitted to our clinic with the complaint of lower abdominal pain, weight gain and abdominal distension of five months' duration. Her menstrual cycles had been regular and the amount of menstrual bleeding was normal. Her past medical and surgical histories were unremarkable. Her family history revealed no clues of colon, breast, endometrium, or ovarian cancer among the first-degree relatives. Pelvic examination revealed a large, irregular, partially mobile right-sided adnexal mass that extended to the pelvic wall and filled the pouch of Douglas. Ultrasound screening revealed a bilateral, heterogeneous solid-cystic adnexal mass with an irregular surface, containing a septum and papillary projections and a large amount of ascites. Doppler ultrasonography showed low vascular impedance. Magnetic resonance imaging showed bilateral, hypodense, multiseptated, 7 x 10 x 8 cm sized masses containing papillary projections. There were no abnormal findings in the bones, stomach, colon, lungs or retroperitoneal lymph nodes. Endometrial biopsy revealed an endometrioid carcinoma with a histologic grade of 2 and nuclear grade of 3. Complete blood count and serum biochemical levels were within normal values. CA125 was elevated to 3005 U/ml.

The patient underwent a laparotomy. Approximately 1500 ml of ascites fluid was found in the abdomen. In intraoperative exploration, the right ovary was enlarged to about 10 x 8 cm in size and the left ovary was enlarged to about 7 x 8 cm in size. The uterus was slightly enlarged. Multiple metastases were

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Fig. 1

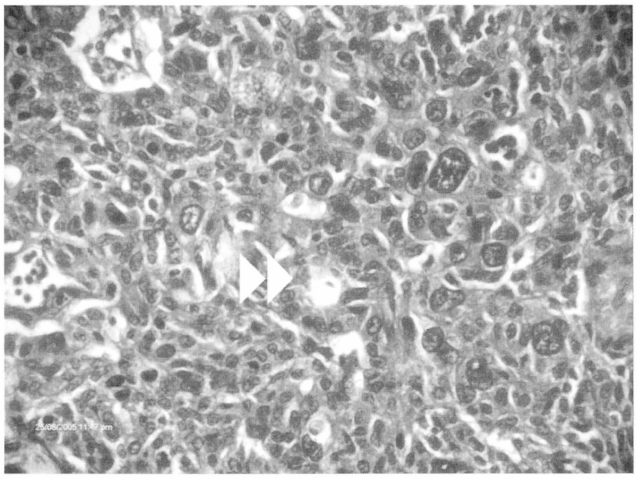
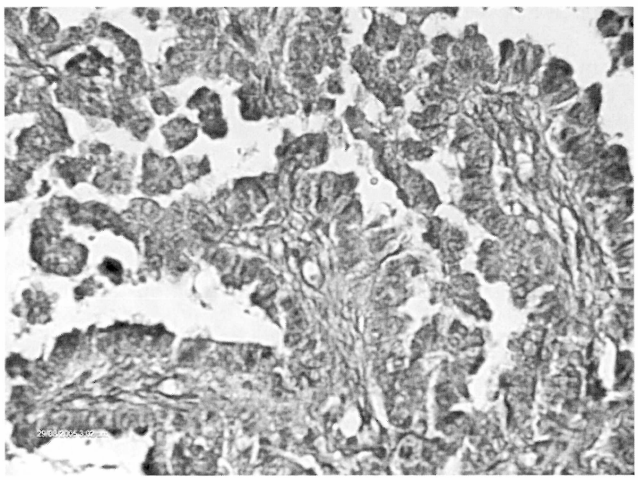


Fig. 3



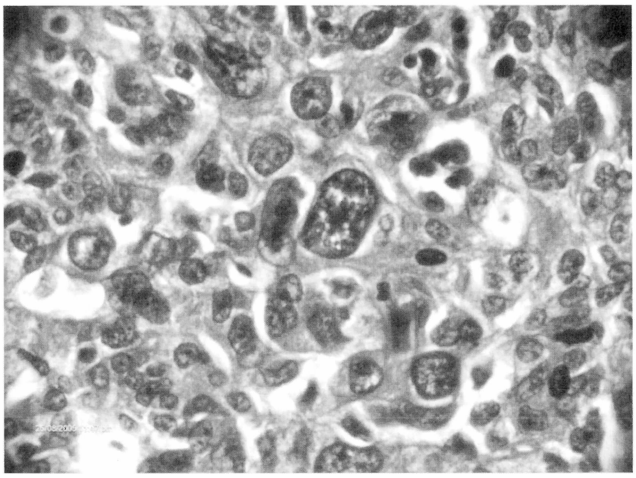


Figure 1: Small gland lumens (arrow) and solid areas (H&E x 40).

Figure 2: Marked nuclear atypia in high grade endometrioid adenocarcinoma (H&E x 100).

Figure 3: Complex papillary arrangement (H&E x 40).

observed on the peritoneal surface, and omentum. There were no palpable pelvic and paraaortic lymph nodes. Total abdominal hysterectomy, bilateral salpingo-oophorectomy, bilateral pelvic and paraaortic lymph node dissection, partial omentectomy, and appendectomy were performed.

On pathologic examination, a polypoid tumoral mass 3.5 x 1.5 x 1.5 cm in diameter arising from the fundal endometrium was seen. The tumor had infiltrated diffusely into one half of the myometrium. In histologic examination, rare gland lumens and solid proliferations of epithelium were seen (Figure 1). The nuclei of the epithelium were markedly enlarged and pleomorphic with large prominent nucleoli and irregular coarse chromatin (Figure 2). The left ovary was 16 x 9 x 6 cm in diameter; the right ovary was 8 x 8 x 2 cm in diameter. In the cut section, both ovaries contained bloody fluid with multilocular soft and friable papillae, filling the cystic cavities. The external surface displayed surface papillae. Some areas were solid, pink to gray in color with less obvious papillae and hemorrhage and necrosis were seen. The tumor displayed complex papillary and focal solid patterns and moderate nuclear atypia with scanty cytoplasm and a high nuclear/cytoplasmic ratio (Figure 3). According to the macroscopic and microscopic findings, pathologic diagnoses of endometrioid carcinoma in the endometrium and serous papillary carcinoma in both ovaries were made.

The final diagnosis was a FIGO Stage III C papillary serous carcinoma of bilateral ovaries and Stage I C endometrial carcinoma of endometrioid type.

Postoperatively, the patient received six courses of chemotherapy consisting of cisplatin and paclitaxel and irraditation therapy. In the follow-up, the patient showed no evidence of recurrence during the 18 months post surgery.

Discussion

Synchronous ovarian primary tumors are infrequently found in patients with endometrial and ovarian cancers [8]. It is difficult to distinguish clinical and pathologic differences between independent primaries of the endometrium and ovary from metastatic endometrial carcinoma. Several clinico-pathologic criteria have been proposed to differentiate these two distinct cancers. The criteria for identification of the synchronous primary cancers include either distinct histologic types (major criterion) or all of the following minor criteria: (1) both tumors confined to primary sites (2) no direct extension between tumors (3) the absence of lymphovascular tumor emboli (4) no or only superficial myometrial invasion (5) the existence of a unilateral ovarian tumor (80-90% of cases) (6) distant metastasis [2, 9]. The majority of clinico-pathologic features are useful; yet, in several cases the tumors do not meet all the differential criteria

and share features of both categories [2, 7, 10]. Since the tumor in our case consisted of two different histologic types, it was easy to determine whether it was a metastatic or an independent primary tumor.

While the etiology of dual primary cancers in the genital tract is still unclear, it has been postulated that the extended müllerian system, comprising the ovarian epithelium, fallopian tube, uterine corpus and cervix, may react as a single morphologic unit to produce primary carcinomas in multiple sites [9]. According to authors, the median age at diagnosis is 50 years in women with synchronous primary cancers of the endometrium and ovary where women who have either endometrial or ovarian cancer are predominantly postmenopausal and the median age of onset is between 60 and 63 years [5, 16]. Familial cancer syndromes account for patients diagnosed with multiple cancers or patients diagnosed with cancers at a young age. Hereditary nonpolyposis colorectal carcinoma (HNPCC) and hereditary breast-ovarian cancer syndrome include gynecologic malignancies. Families with HNPCC have an increased lifetime risk of endometrial (40%), ovarian (10%) carcinomas and a predisposition to synchronous tumors [16]. Lynch and colleagues described a series of 80 patients with ovarian cancer from HNPCC families and reported that 21.5% of them had synchronous cancers at diagnosis [17]. However, this possible inheredited predisposition could not be detected by routine family history in the present case.

Obese women are at an increased risk for endometrium cancer because of the hyperestrogenic state. Yet, the relation between obesity and ovarian cancer is still unclear. England et al. reported that women who were overweight or obese in young adulthood were found to be at a high risk for ovarian cancer [11, 12]. In addition, the synchronous primary cancers appeared in women who had a body mass index (BMI) > 25. In general 33% of patients were nulliparous. According to Soliman, 40% of patients with synchronous endometrioid/serous tumors were nulliparous [5]. Women with synchronous primary cancers of the endometrium and ovary had distinct clinical characteristics including young age, obesity, premenopausal status and nulliparity; however, the patient in our case was multiparous and had a normal BMI.

The most common symptom of synchronous cancers is abnormal uterine bleeding (56.2%) [4]. Seventeen percent of patients have abdominal and pelvic pain and 13% of patients have an abdominal or pelvic mass [4, 5]. However, our patient presented with complaints of lower abdominal pain, weight gain and abdominal distension.

The majority of primary carcinomas of the uterus and ovary are well differentiated and of endometrioid cell type. Some of them are of either mucinous or serous differentiation in both sites. Patients rarely have endometrioid carcinoma of the endometrium and clear cell carcinoma of the ovary [1, 5, 6] (Table). Our patient had a Stage III C bilateral papillary serous carcinoma of the ovaries and Stage I C endometrial carcinoma of endometrioid type.

Table 1. — *Histologic types of ovarian and endometrial tumors*

Reference	Total number of cases	Histologic type Ovary	Endometrium	Number of cases
Richard *et al.* [6]	74	Endometrioid	Endometrioid	38
		Mucinous	Endometrioid	1
		Mucinous	Mucinous	2
		Serous	Endometrioid	1
		Serous	Serous	2
Pearl *et al.* [6]	26	Endometrioid	Endometrioid	12
		Endometrioid	Mucinous	1
		Clear cell	Clear cell	1
		Transitional	Endometrioid	1
Soliman *et al.* [1]	84	Endometrioid	Endometrioid	57
		Clear cell	Endometrioid	7
		Serous	Endometrioid	11
		Other		9
Present case	1	Bilateral serous	Endometrioid	1

Patients with synchronous primary cancers have a higher chance of survival than those with metastatic diseases. Furthermore, synchronous primaries show better survival rates than single aggressive ovarian cancers. This may be due to the detection of patients at earlier clinical stages and lower graded disease stages [3]. The patients with grade 1 endometrioid tumors who are only treated with surgery show no recurrences [1, 9, 13]. In contrast, patients with higher graded ovarian tumors are usually treated with adjuvant chemotherapy or irradiation. In addition, the nonendometrioid or dissimilar histologic types, which often present with deep myometrial or ovarian hilar invasion and pelvic or abdominal metastases, may be aggressive and show poor prognosis [1, 14]. Our patient received six courses of chemotherapy and irradiation therapy. During the follow-up, the patient has shown no evidence of recurrence 18 months after surgery.

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