A case with three primary tumors of the ovary, endometrium and gallbladder

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Summary

A case with three synchronous tumors is presented. A 52-year-old patient underwent a total abdominal hysterectomy with bilateral salpingo-oophorectomy, bilateral pelvic and paraaortic lymph node dissection, and partial omentectomy for endometrial carcinoma accompanied by an adnexal mass. She further underwent cholecystectomy for a perioperative incidental suspicious nodule on the serosal surface of the gallbladder. Histopathology revealed a uterine endometrioid adenocarcinoma, a mucinous adenocarcinoma of the gallbladder, and an ovarian endometrioid carcinoma with a clear cell component. The progress of the patient until the time of death is discussed.

Key words: Endometrial carcinoma; Ovarian carcinoma; Gallbladder carcinoma; Synchronous tumor.

Introduction

The synchronized association of ovarian and endometrial tumors is not a rare occurrence among female genital cancers. While this may be due to metastasis, it can also be a primary neoplasm originating from two different tissues. These two events present with different clinical profiles and prognoses. The combination of different primary cancers is observed more rarely than metastatic cancers; however, they generally have a better prognosis.

The etiology of synchronous cancers is yet unknown. Tissues with the same embryological origins are believed to respond in a similar fashion to carcinogens [1, 2]. However, in contrast, synchronous cancers may be observed in separate tissues, as observed in the present case.

In the present report, we discuss a patient with three synchronously occurring tumors, i.e., a uterine endometrioid adenocarcinoma, a gallbladder mucinous adenocarcinoma, and an ovarian endometrioid carcinoma with a clear cell component.

Case Report

A 52-year-old patient (gravida, 5, parity, 3, abortion, 2) was admitted to an outpatient clinic in December 2004 due to menometrorrhagia. She had a past history of appendectomy performed 20 years ago. Endometrial biopsy revealed endometrioid adenocarcinoma, and a heterogeneous mass measuring 20 × 11 cm was observed in the right adnexal space. She was referred to the Department of Obstetrics and Gynecology, Uludag University Medical Faculty. She had been menstruating at intervals of 30 to 90 days with excessive bleeding lasting for ten days during the previous six months. The patient had no significant family history.

Gynecological examination revealed a semi-mobile mass originating from the right side, occupying the pelvis, and extending to the umbilicus that made the uterus nonpalpable. Ultrasonography showed a mass with cystic components that pushed the bladder anteriorly. Localized ascitis was observed lateral to the adnexal mass and uterus on the right side. Upper abdominal and thoracic tomographies and mammography were normal. Cystoscopy was performed and a biopsy was taken from the suspicious area at the bladder neck. Histopathological examination revealed squamous metaplasia. The serum CA125 level was 170.3 U/ml; CA15-3, 51.6 U/ml; CA19-9, 33.7 U/ml; and CEA, 1.76 ng/ml.

Laparotomy was performed with the diagnosis of endometrial carcinoma. In the right adnexal area, a smooth-surfaced cystic mass measuring 18 × 13 cm was observed. Adhesions were present between the mass and the omentum. The left adnexal area and the uterine size were normal. During the examination of the upper abdomen, the gallbladder was observed to be completely filled with multiple stones. Moreover, there was a grayish-pink nodule measuring 1.5 × 1.0 cm on the peritoneum covering the neck of the gallbladder. Total abdominal hysterectomy with bilateral salpingo-oophorectomy, bilateral pelvic and paraaortic lymph node dissection, partial omentectomy, and cholecystectomy were performed.

Macroscopically, the right ovarian cystic mass measured 15 × 11 × 7 cm. Dissection of the cyst showed that it had a multicystic pattern with solid areas of a maximum of 4 cm in size. Microscopically, the atypical cells were polygonal or oval shaped with vesicular nuclei, prominent nucleoli, and eosinophilic cytoplasm, and were intermingled with solid areas of atypical epithelial cells with large vesicular nuclei (Figure 1). Tumor cells were strongly and diffusely positive for CK7 and were negative for CK20, CA125, and CA19-9 in immunohistochemical staining. Examination of the right ovary, which had an intact surface, revealed endometrioid carcinoma with a clear cell component and no tumor cells were observed in the left ovary.

Macroscopically, the endometrial cavity was occupied with a grayish-pinkish-brownish fragile tumor tissue measuring 3.0 × 8.6 cm, with polypoid extensions into the endocervical canal. The maximum depth of invasion was 1.3 cm of the whole wall thickness that measured 3.0 cm. Microscopically, the tumor tissue had grown with polypoid extensions into the luminal

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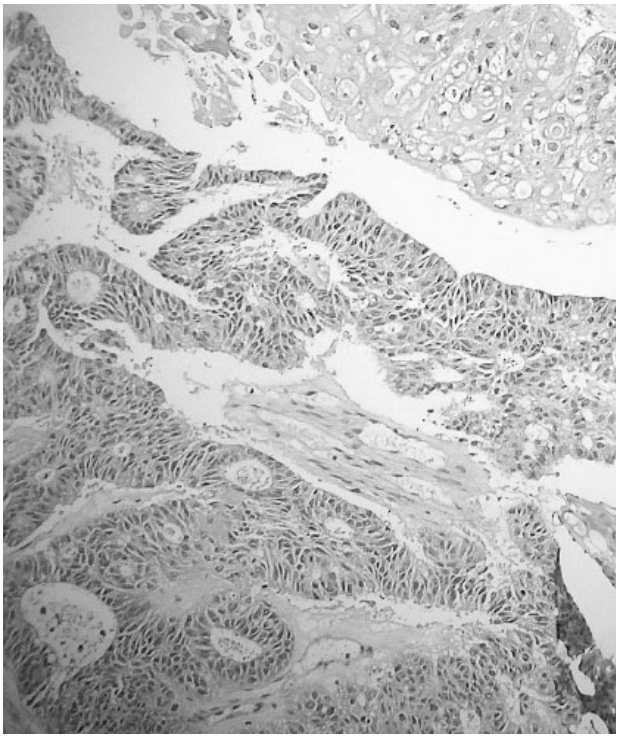

Figure 1. — Hematoxylin-eosin stained section of the ovarian tumor (x 100).

surface and had invaded subepithelial stroma with glandular cribriform structures. The tumor was comprised of atypical oval or columnar epithelial cells with large vesicular nuclei and eosinophilic cytoplasm (Figure 2). Lower uterine segment involvement and superficial invasion of the cervical stroma were observed. The histopathological examination reported grade 1 endometrioid adenocarcinoma.

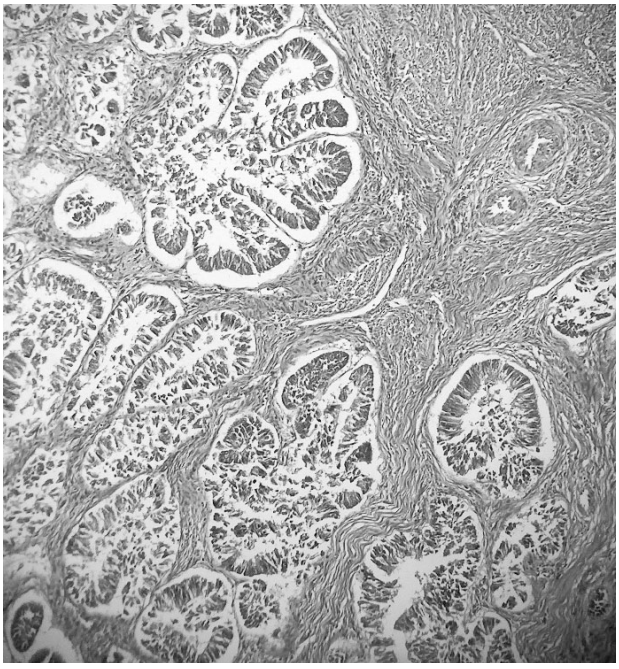

Figure 2. — Hematoxylin-eosin stained section of the endometrial tumor (x 40).

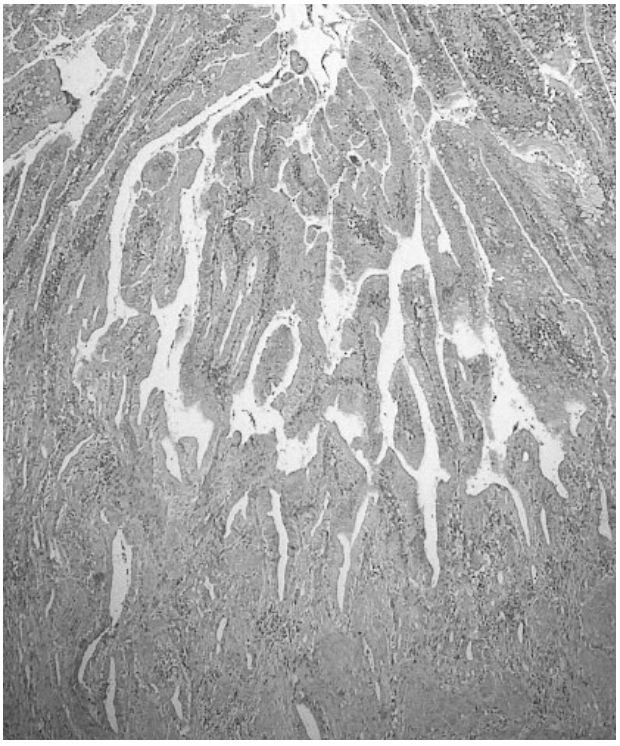

Figure 3. — Hematoxylin-eosin stained section of the gallbladder tumor (x 40).

Macroscopically, a grayish-pinkish area measuring 1.5 × 1.2 cm was present on the peritoneal surface of the gallbladder neck. Dissection revealed nodular thickening on the corresponding side along with the presence of multiple stones. Microscopically, the tumor was observed to infiltrate the whole thickness of the gallbladder wall and was comprised of atypical oval or columnar epithelial cells with vesicular nuclei, prominent nucleoli, and eosinophilic cytoplasm; these cells formed adenoid and cribriform structures with extracellular mucin accumulations. Adjacent to the tumor tissue, atypical changes and metaplasia were observed within the surface epithelium. There was no perineural, venous vascular, or lymphatic invasion (Figure 3). Mucin was observed to stain with PAS and mucin stains. Immunohistochemical staining demonstrated that tumor tissue was strongly and diffusely positive for CK7, focally positive for CK20, and negative for CA19-9 and CH25. Histopathological diagnosis was mucinous adenocarcinoma of the gallbladder.

Peritoneal washing samples, the omentum, and pelvic and paraaortic lymph nodes were tumor-free in cytopathologic and histopathologic examination. The patient was diagnosed with ovarian endometrioid carcinoma with a clear cell component, endometrial endometrioid adenocarcinoma, and mucinous adenocarcinoma of the gallbladder.

There were no postoperative complications, and she was administered six courses of PAC (cisplatin, 50 mg/m^2; adriamycin, 50 mg/m^2; cyclophosphamide, 750 mg/m^2) chemotherapy. She responded to the chemotherapy; follow-up examinations included abdominopelvic and thoracic computerized tomography, whole body scintigraphy, and serum tumor marker levels. Pelvic computerized tomography in November 2005 revealed thickening of the rectal wall. At that time, the serum CA125 was 419.7 U/ml; CA15-3, 15.6 U/ml; CA19-9, 14.4 U/ml; CEA, 59.2 ng/ml; and AFP, 1.97 ng/ml. The patient refused any further investigations and did not attend follow-up

examinations for 16 months. In March 2007, she was admitted to our outpatient clinic with the complaint of vaginal bleeding for the previous three months. Gynecological examination revealed an ulcerated, bleeding, infiltrative mass on the vaginal cuff measuring 3 × 4 cm. The result of the biopsy reported endometrioid adenocarcinoma. Computerized tomography revealed a single suspicious metastatic nodule in the right lung parenchyma, a 5 × 5 cm metastasis in the spleen, conglomerated lymph nodes around the head of the pancreas, and urinary bladder invasion with a tumor mass measuring 3 × 6 cm in the pelvis. Radiotherapy was planned as further treatment; however, the patient died.

Discussion

The synchronous formation of tumors originating from different tissues is rather rare. While the incidence of synchronous endometrial tumors for patients with ovarian tumor varies between 1.6% and 67%, the incidence of ovarian tumors in patients with endometrial cancer varies between 0.7% and 10% [3-5]. Synchronous ovarian and endometrial cancers are generally of metastatic character; moreover, the endometrium is a common site of metastasis for ovarian carcinomas.

The difficulty in dealing with synchronous tumors is differentiating the origin of the tumor, i.e., whether they are of primary or metastatic character. Synchronous cancers are most commonly metastatic in nature. The ovary often harbors metastatic gastrointestinal tract (GIT) tumors. The most common GIT tumor metastases originate from the stomach and the colon; those from the gallbladder are rare [6]. Differences between the histological patterns are the most important criteria in differentiating the primary or metastatic properties of tumors. Restriction of the tumors to their primary site, absence of any direct relation between the two tumors, absence of lymphovascular invasion, either absence or superficial presence of myometrial invasion, and absence of metastasis can all be used as minor criteria [7-10].

In our case, three different histological patterns, namely, endometrioid with a clear cell component, endometrioid, and mucinous pattern were observed. In the gallbladder, the surgical margins were tumor free, there was no serosal involvement of the ovary, and the invasion of the endometrium corresponded to less than half of the myometrium. There was no lymphovascular invasion or lymph node metastasis; moreover, the peritoneal cytology was negative. The patient was diagnosed as having three synchronously occurring tumors in the uterus, ovary, and gallbladder.

The prognosis in synchronous primary cancers is known to vary considerably [11]. Some authors have suggested that women diagnosed with synchronous primary cancers have a better overall prognosis than if their disease is classified as single-organ disease with metastases. This may be due to the increased chance of early diagnosis since the patient may have more than a single symptom and thereby seek medical help. Our patient would have been diagnosed in the advanced stages of gallbladder or ovarian cancer if she had not experienced bleeding due to endometrial cancer.

Our experience with this case shows that synchronous tumors of ovary, endometrium and gallbladder can be managed with appropriate chemotherapy.

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