Research Letter

Synchronous primary ovarian granulosa cell tumor and endometrial cancer

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Accepted 18 November 2010

Synchronous primary tumors of the genital tract are rare [1]. The rate of synchronous gynecological malignancies is 0.7–1.8% in patients with gynecological tumors [2]. Primary tumors of the ovary and endometrium are the most common synchronous tumors of the female genital tract [3]. This report describes a case of synchronous granulosa cell tumor (GCT) and endometrial cancer in a 73-year-old woman.

A 73-year-old, gravida 9, para 9, female presented having experienced significant vaginal bleeding for 1 month. Her menarche began at age 14 and menopause began at age 53. She had a history of diabetes mellitus and hypertension for over 10 years and had not taken contraceptives or hormone replacement therapy. Examination using ultrasonography revealed an enlarged uterus with an irregular echogenic lesion measuring 4.0 × 4.2 × 4.7 cm in the uterine cavity. A hypoechoic right adnexal complex tumor measuring 5.4 × 4.9 cm (Fig. 1) was also identified. The cancer antigen 125 (CA-125) concentration was 16.1 U/ml (normal range, <35.0 U/ml). Endometrial biopsy was positive for adenocarcinoma. Magnetic resonance imaging (MRI) identified a heterogeneous enhanced tumor mass invading the deep myometrium of the corpus uteri. Additionally, a heterogeneous enhanced multilocular massive right adnexal mass (8.0 × 4.4 cm) with both cystic and solid components (Fig. 2) was demonstrated.

Based on a clinical diagnosis of endometrial cancer and a right ovarian tumor, the patient underwent a total abdominal hysterectomy, bilateral salpingo-oophorectomy, bilateral pelvic and para-aortic lymphadenectomy, omentectomy, peritoneal biopsies and pelvic washings. Fig. 3 shows the uterus and right ovary. A cut section of the granulosa cell tumor was grayish white, reflecting its lipid content. Hemorrhage in multiseptate cysts was also noted (Fig. 3). Pathological findings revealed moderately differentiated endometrioid adenocarcinoma (stage IB) of the uterus, and a grade 2 right ovarian granulosa cell tumor (stage IA). Peritoneal cytology and lymph nodes were negative for malignant cells. Radiotherapy was planned; however, the patient chose not to receive this treatment.

Synchronous primary gynecological tumors are typically detected in relatively old, overweight, multiparous and postmenopausal women, such as this patient, with a history of diabetes or hypertension [4]. Synchronous primary tumors of the endometrium and ovary should have a better prognosis than endometrial or ovarian cancer alone, as synchronous tumors are typically diagnosed during the early stages of disease and are low grade [4].

This patient presented with a synchronous ovarian granulosa cell tumor and endometrial adenocarcinoma. In this case, old age, multiparity and obesity (body mass index, 32.2 kg/m²) were noted. The CA-125 concentration at 16.1 U/ml was within the normal range (<35.0 U/ml). Preoperative MRI study identified typical features of a GCT, such as a sponge-like multilocular cystic mass [5, 6]. In such patients, a thickened endometrium is common, as was the case in our patient. Other evidence of hyperestrogenism, such as breast tenderness and menstrual abnormalities in premenopausal women, are sometimes present. Clinical and imaging findings give clues for the suspicion of estrogen-producing ovarian tumors such as GCTs. A cause-and-effect relationship exists between these two primary tumors.

GCT is the most common estrogenic ovarian tumor, accounting for 5% of all ovarian cancers [7]. Perhaps due to persistent hyperestrogenism, a wide spectrum of endometrial pathology ranging from a polyp to endometrial hyperplasia and carcinoma has been documented [7–9]. Endometrial cancer has been reported in 5–10% of these patients [10,11] and most synchronous endometrial cancers are well-differentiated, early-stage endometrial adenocarcinomas [12].
Notably, there are adult and juvenile forms of GCTs. Adult GCTs are common in women who are obese (body mass index $>$30), and have a family history of breast or ovarian cancer [13]. The risk is decreased for women who take oral contraceptives, are current or past smokers, and those who are parous. Adult GCTs occur primarily during the perimenopausal years, with patients having a mean age of 51–57 years at presentation [8]. While some GCTs have been reported in subjects aged $\geq$70, some were tumors that had recurred decades after the initial surgical excision [14–16]. Compared with epithelial ovarian malignancies, GCTs typically present at a younger age, with a peak occurrence when patients are aged 50–60 years [17]. GCTs can, however, be seen in patients of advanced age.

Ultrasound findings (a septated cystic or solid mass related to the ovary) are typically nonspecific and MRI is more informative, showing the typical features of a sponge-like multilocular cystic mass filled with blood clots [5,6]. While the diagnosis is based on pathological findings, GCT should be suspected preoperatively based on the presence of an adnexal mass combined with signs of excess estrogen or androgen. The possibility of an estrogen-producing tumor, such as a GCT, should be considered in women aged $>$50 years with vaginal bleeding who are not on hormone therapy and who have an ovarian tumor. The principal therapy for synchronous tumors is surgical resection based on the ovarian cancer protocol and close follow-up after surgery.

Fig. 1. Ultrasonography findings of an adult granulosa cell tumor of the right ovary and endometrial cancer. (A) An echogenic septated cystic mass over the right ovary measuring $5.4 \times 4.9$ cm. (B) An enlarged uterus with an irregular echogenic lesion of the uterine cavity measuring $6.7 \times 4.6$ cm.

Fig. 2. MRI findings of the adult granulosa cell tumor. (A) Coronal T2-weighted image (T2WI), (B) coronal T1-weighted image (T1WI) and (C) a coronal contrast-enhanced and fat-saturated T1-weighted image (CEFST1WI). A multilocular cystic mass with relatively thick septa (arrowhead) is demonstrated on T2- and T1WI (A and B, arrows). The septa show hypointense contrast on the T2WI (A) and intense contrast enhancement (C).
Fig. 3. Gross picture of the uterus (A) and right ovary (B). A cut section of granulosa cell tumor was grey white, reflecting its lipid content. Hemorrhaging of multiseptate cysts was also presented.

References