CASE REPORT

Coexistence of Ovarian Cancer and Renal Cell Carcinoma

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Coexistence of ovarian cancer and renal cell carcinoma (RCC) is extremely rare. Only one case was diagnosed in a total of 584 patients with RCC from 1982 to 2002 at our hospital. A 58-year-old woman presented with an enlarged girdle length for 3 months. Computed tomography scan showed a right cystic adnexal mass measuring 10 × 10 cm, and another tumor measuring 3 × 2 cm at the right kidney. She underwent debulking surgery and radical nephrectomy. Pathologic examination revealed right ovarian clear-cell carcinoma with peritoneal, omental, and fallopian tube metastasis, and conventional clear-cell renal carcinoma. RCC was strongly positive in epithelial membrane antigen (EMA) staining and negative in estrogen receptors (ER), progesterone receptors (PR), 34βE12 (high molecular weight cytokeratin), and vimentin staining. Ovarian clear-cell carcinoma showed weakly positive results in EMA staining and negative results in ER, PR, 34βE12, and vimentin staining. Although chemotherapy was given, the patient died of disseminated ovarian cancer metastasis 20 months after operation. In conclusion, coexistence of RCC and ovarian cancer is rare and the pathogenesis remains to be clarified. [*J Formos Med Assoc* 2007;106(3 Suppl):S15–S19]

Key Words: ovarian cancer, renal cell carcinoma, synchronous tumors

Coexistence of double primary cancers in the same patient is rare. Myoga et al reported the first case of synchronous primary ovarian cancer and renal cell carcinoma (RCC) in 1988.[1] To date, only sporadic cases have been reported. Despite the fact that the association between RCC and steroid-hormone target organs (breasts, uterus, ovaries) has been described, the pathogenesis of such disease is unclear. The clinical differentiation between double primary and metastatic tumors remains difficult. Therefore, we report a case diagnosed with coexistence of double primary cancers involving the right ovary and right kidney.

Case Report

A 58-year-old G6P4 woman presented with an enlarged girdle length for about 3 months. She had menarche at the age of 13 and went through menopause at the age of 55. She had never undergone hormone replacement therapy. Abdominal sonography and computed tomography (CT) showed a right cystic adnexal mass measuring 10 × 10 cm, and another well-defined tumor about 3 × 2 cm at the right kidney (Figures 1 and 2). The CA-125 serum level was 80.8 U/mL (normal, < 35 U/mL). The patient then underwent

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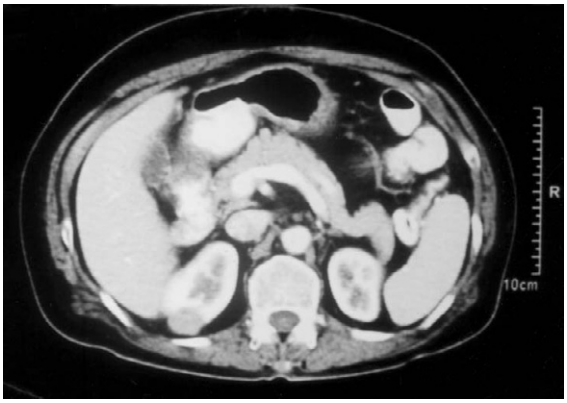

Figure 1. A 2.4-cm well-defined tumor mass at the right kidney with mild enhancement.

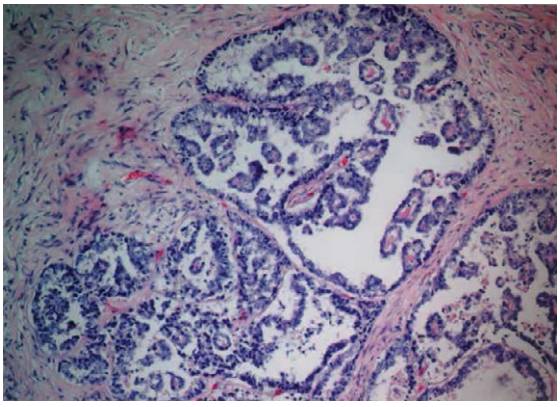

Figure 3. Clear-cell carcinoma of the ovary with tubular and tubulopapillary growth pattern (hematoxylin & eosin, 100×).

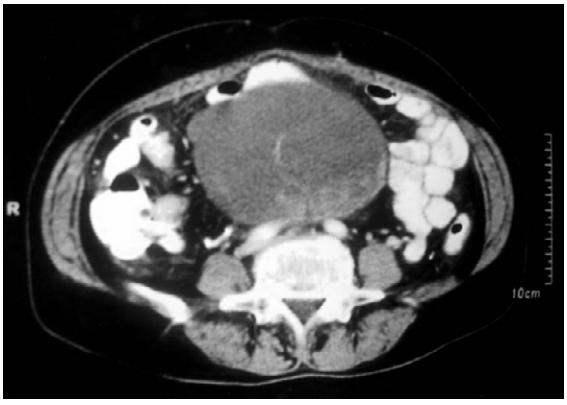

Figure 2. Huge adnexal cystic tumor (15 × 14 × 17.5 cm) is noted with heterogeneous peripheral enhancement.

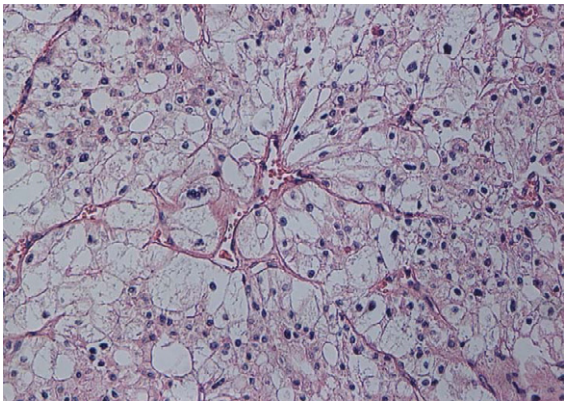

Figure 4. Conventional clear-cell-type renal cell carcinoma (hematoxylin & eosin, 100×).

debulking surgery (total abdominal hysterectomy with bilateral salpingo-oophorectomy, pelvic lymph node dissection, and omentectomy) for the ovarian cancer and radical nephrectomy for the right renal tumor. Pathology revealed right ovarian clear-cell carcinoma with peritoneal, omental, and bilateral fallopian tube metastasis (Figure 3), along with conventional clear-cell-type RCC without evidence of extrarenal involvement (Figure 4). Immunohistochemical staining for RCC showed strongly positive results in epithelial membrane antigen (EMA) staining and negative results in estrogen receptor (ER), progesterone receptor (PR), 34βE12, and vimentin staining. Ovarian clear-cell carcinoma showed weakly positive results in EMA staining and negative results in ER, PR, 34βE12, and vimentin staining. The pathologic staging was pT1N0M0 for RCC, and stage IIIC (pT3cN0M0) for ovarian cancer.

The patient's postoperative CA-125 level was 5.2 U/mL. After completing six courses of adjuvant chemotherapy with paclitaxel and carboplatin, tumor recurrence with multiple liver and lung metastases was found by CT scan. The chemotherapy regimen was then shifted to liposomal, doxorubicin, and carboplatin for three courses. However, a poor response was noted. The patient died of disseminated metastasis due to ovarian cancer about 20 months after operation.

Discussion

Multiple malignancies in the same patient have been reported to present in 1.84–3.9% of all

cancers.[2] Coexistence of double primary tumors in one individual is extremely rare. Einer et al reported 30 years of data that included 3863 cases of female gynecologic malignancies. Among them, 26 (0.7%) patients with synchronous primary cancers were identified. The most frequent coexistent tumors were ovarian and endometrial cancers. Cases of primary ovarian and RCC were not identified in that study.[3,4] Myoga et al published the first case of synchronous primary ovarian and renal cancers in 1988.[1] To date, only sporadic cases have been reported.

The pathogenesis for synchronous malignancies in the same patient is not entirely clear. However, common etiologies, such as exposure to the same hormone or carcinogen, are often suspected.[5] Some RCCs have been thought to be hormone dependent. The association between RCC and steroid-hormone target organs (breasts, uterus, ovaries) may be explained by such a hypothesis. Di Silverio et al reported 17 cases of RCCs associated with second primary neoplasms occurring in steroid-hormone target tissues. Among them, 10 RCCs were associated with breast carcinoma, four with endometrial carcinoma, and only three with ovarian carcinoma.[6] We reviewed the data in our hospital, and only one patient was noted to have coexistence of ovarian cancer and RCC out of a total of 584 patients with RCC from 1982 to 2002.

In recent years, several authors have studied steroid-receptor molecules in kidneys. Bath et al demonstrated the presence of estradiol receptors in hamster kidneys.[7] Bullock and Bardin revealed the existence of androgen receptors in mouse kidneys.[8] The cytosol from normal human kidney specimens showed binding activity for steroid hormones, which was related to a receptor specific only for estradiol and progesterone.[9]

Several reports have described the presence of androgen receptors, ER, and PR, in RCC tissue.[10,11] In addition, chronic administration of estradiol or diethylstilbestrol to male Syrian hamsters induced kidney tumors, and simultaneous administration of the antiestrogen nafoxidine completely inhibited tumor formation.[12] Banerjee et al also found that estradiol induced the development of micronuclei and aneuploidy in renal tissue.[13] How estrogen induces tumorigenesis in the kidney remains to be clarified. However, we did not detect the presence of ER and PR in the RCC of our case.

The relationship among reproductive factors, steroid hormones, and RCC has been studied in international investigations carried out between 1989 and 1991 on 608 women with RCC and 766 female controls.[14,15] A significant trend in the risk of developing RCC is associated with the number of births, with an excessive 80% risk being found in six or more births as compared with one birth. A decreased risk was found for increasing age at menarche and for increasing age at the first birth; in contrast, the age at menopause or estrogen-replacement therapy was unrelated to the risk of developing RCC. Our patient had menarche at the age of 13 and went through menopause at the age of 55. Her reproductive history was G6P4, and she had no history of exogenous hormone replacement therapy. Her age during the first delivery was 21. In this regard, she would have been expected to be at risk for developing RCC in terms of menstrual and reproductive history.

Metastasis is often determined if synchronous tumors have similar histologies. To make a definitive diagnosis of coexistent double tumors, distinctively different histologies should be observed. In 1932, Warren and Gates described criteria for making a diagnosis of coexistent primary tumors. These criteria included the following: (1) each of the tumors must present a definite picture of malignancy; (2) each tumor must be distinct; (3) the probability of one tumor being a result of metastasis of the other must be excluded.[2] However, the differentiation between metastatic tumors and double primary tumors sometimes poses a diagnostic challenge. In our case, the patient's ovarian cancer was clear-cell carcinoma with a tubular and tubulopapillary growth pattern. The kidney showed a conventional clear-cell renal carcinoma. The pathology distinguished between the two primary tumors clearly, excluding the possibility of

metastasis. In general, the presence of a solid or tubular growth pattern comprising clear cells within a prominent vascular network was the histologic characteristic of clear-cell-type RCC. However, ovarian clear-cell carcinoma showed clear cells with frequent hobnail appearance, which were arranged in tubules and occasional cystic change. The clear cells may line complex papillae variably containing periodic acid-Schiff-positive hyaline basement membrane material expanding the papillary cores. If the differentiation in histology is not clear, immunohistochemical staining with a panel of antibodies, including cytokeratins (CK5, CK6, CK7), ER, PR, vimentin, EMA, CA-125, 34βE12, CD10, and RCC antibody could be helpful. In general, RCCs, particularly the clear-cell types, demonstrate a weakly positive or negative staining for cytokeratins (CK5, CK6, CK7), 34βE12, CA-125, PR, and ER but demonstrate positive staining for vimentin and RCC antibody. Some RCCs can show a coexpression of both cytokeratins and vimentin. Ovarian clear-cell carcinoma is usually positive for PR, ER, and CA-125 but negative for 34βE12 and vimentin.[16] In our case, RCC staining showed strongly positive results in EMA staining and negative results in CK, ER, PR, 34βE12, and vimentin staining. Ovarian cancer showed weakly positive results in EMA staining and negative results in CK, ER, PR, 34βE12, and vimentin staining. CD10 was used to reliably distinguish RCC of clear-cell and papillary types. Some reported the utility of CD10 in the diagnosis of metastatic RCC by fine-needle aspiration biopsy but the diagnostic usefulness is limited because of its low specificity.[17]

Preoperative diagnosis to differentiate between coexistent double cancers and metastasis may be difficult. In preoperative imaging studies (CT or MRI), renal metastases are usually small, multiple, bilateral, wedge-shaped, less exophytic, and are located within the renal capsule. In contrast, primary RCC is usually single, unilateral, nonwedge-shaped, and exophytic, as seen in our case.[18]

Although extremely rare, the possibility of coexistent RCC and ovarian cancer should be considered in clinical practice. Careful attention should be paid to the differential diagnosis between double primary and metastatic tumors, based on the pathologic and clinical characteristics.

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