

Triple Synchronous Primary Ovarian, Endometrial And Breast Cancer: A Case Report**Üçlü Senkron Primer Over, Endometrium ve Meme Kanseri: Bir Olgu Sunumu**Kadir ÇETİNKAYA¹,
Ebru YÜCE², <https://orcid.org/0000-0003-4490-8267> <https://orcid.org/0000-0003-4907-7730>¹ Ankara Oncology Education and Research Hospital, Department of Gynecology and Obstetrics, Ankara, Turkey² Ankara Liv Hospital, Department of Gynecology and Obstetrics, Ankara, Turkey**ÖZ**

Tümörlerin teşhisleri arasındaki süreye bağlı olarak, multipl primer maligniteler senkron ve metakron tümörler olarak bilinir. Senkron kanserler, aynı anda veya ilk maligniteden sonra 6 ay içinde ortaya çıkan sekonder tümörlerdir.

Sunduğumuz hastamız ilk önce meme kanseri tanısı aldı ve 3 ay sonra endometrium kanseri tespit edildi. Evreleme cerrahisi sırasında ise over kanseri tanısı konuldu.

Anahtar kelimeler: Senkron kanser, over, endometrium, meme.

ABSTRACT

Multiple primary malignancies are known as synchronous and metachronous tumors depending on the interval between tumor diagnosis. Synchronous cancers are secondary tumors occurring simultaneously or within 6 months after the first malignancy. We present a case that breast cancer was diagnosed firstly, and then endometrial cancer was diagnosed after 3 months and at the time of the staging surgery for endometrial cancer she was diagnosed with ovarian cancer.

Keywords: Synchronous cancer, ovarian, endometrial, breast.

INTRODUCTION

Synchronous tumors are defined as two or more tumors occurring in a patient simultaneously (1). Synchronous multiple primary tumors of the female genital tract are well-known phenomenon, comprising only 1% to 6% of all genital tract neoplasms (1). Synchronous primary cancers of the endometrium and ovary are found in 5% of women with endometrial cancer and 10% of women with ovarian cancer (1).

In this report, we present the clinical and pathological findings of a 63 years-old patient with concomitant ovarian, endometrial and breast cancer.

CASE REPORT

A 63-years-old, gravida 1, parity 1 woman was admitted to the Obstetrics and Gynecology outpatient clinic for routine menopause examination. The mammogram revealed a suspicious mass with a nodular density 15x13 mm in the upper-outer quadrant of the left breast. The breast ultrasound revealed a 16x11.1 mm part lobule contoured mass on the left breast at two o'clock position, 35 mm far and 6.8 mm deep from the areola. Axillary lymph nodes were negative bilaterally. Subsequent fine-needle aspiration biopsy reported a suspicious malignancy, and tru-cut biopsy diagnosed an invasive breast carcinoma. ER positivity was 100%, PR positivity was 40%. The score of Cerb-B2 was 0, and Ki-67 positivity was 30%. There was no in-situ component

in specimen. One month later patient has undergone left breast conserving surgery and intraoperative radiotherapy. Sentinel lymph node biopsy was negative. The pathological diagnosis was grade 2 ductal carcinoma. Tumor diameter was 2.8 cm with positive surgical margins. ER, PR, Cerb-B2 and Ki-67 positivity were 90%, 80%, 0, 20%, respectively. There was no lenfovascular invasion. The stage was pNmicT2+M0 Stage II. Letrozole 2.5 mg was started. In PET CT, the involvement was seen in uterus. Transvaginal ultrasonography showed 22x5 mm heterogenous lesion at endometrium and 23x12 mm lesions in right ovary. After medical oncology consultation the endometrial biopsy was performed and the pathological diagnosis was non-endometrioid serous carcinoma type II. After the staging surgery; the diagnosis was serous type II endometrial carcinoma and invasion in the left ovary, left tuba uterina and right fimbria, and primary ovarian granulosa cell tumor in the right ovary. The stage was FIGO IIIB. After 4-month she received 6 courses of Carboplatin and Paclitaxel. Then 50 Gy pelvic RT and two sessions of intracavitary RT were performed for endometrial cancer. After 4 months of treatment Ca-125 level was 366 U/ml. The thoraco-abdominal CT revealed pulmonary nodules and metastases in the liver. PET-CT revealed metastatic lesions in the abdomen and pelvis. Three cycles of topotecan were administered. Chemotherapy was postponed due to leukopenia. Megace 3x160 mg was planned. One month later she was hospitalized for supportive therapy for ascite. She was consulted to neurology clinic due to fatigue and she was diagnosed with common sensorymotor polyneuropathy. Patient died one month later due to the terminal phase of the disease.

Yazışma Adresi/Correspondence Address:

Kadir Çetinkaya

Associate Professor of Gynecology and Obstetrics Ankara Oncology Education and Research Hospital

Tel/Phone: 0505 388 44 13

E-mail: kacetinkaya@gmail.com

Geliş Tarihi : 02.06.2017

Kabul Tarihi : 15.07.2017

DISCUSSION

Multiple primary malignancies can be divided into two categories such as synchronous and metachronous tumors depending on the interval between tumor diagnosis. Synchronous cancers are secondary tumors occurring simultaneously or within 6 months after the first malignancy; metachronous multiple malignancies are secondary cancers that developed after more than 6 months from the first malignancy (3). In our case, breast cancer was diagnosed firstly, and then endometrial cancer was diagnosed after 3 months and at the time of the staging surgery for endometrial cancer she was diagnosed with ovarian cancer. Thus the final diagnosis of our case was synchronous triple primary malignancies.

The mechanisms of multiple primary cancers are not clear and the genetic susceptibility, the immune system of patients, and the intensive exposure to carcinogens including chemo- and/or radiotherapy used in the treatment of tumors thought to be responsible for the development of cancer. It is suggested that the treatment used for the first malignancy has resulted in some damage of specific regions of DNA with chromosome rearrangement or loss responsible for tumorigenesis (2). A secondary malignancy could be defined as a new cancer that occurs as a result of previous treatment with radiation or chemotherapy. The role of hormone therapies must be considered at developing secondary malignancies, too (3).

Genetic susceptibility and the carcinogenic effect of radio/chemotherapy have been largely proposed for the development of secondary malignancies. It is known that people with a family history of cancer will inherit genetic cancer susceptibility as a risk factor and moreover, patients treated and survivors of earlier cancers with genetic susceptibility have an increased risk of multiple primary malignancies (2). There was no family history of our case.

Synchronous tumors are defined as two or more tumors occurring in a patient simultaneously (1). Synchronous carcinoma of ovary and endometrium is the most common with an incidence of 10% of the patients with ovarian cancer (1). In the literature, a few cases with synchronous multiple primary gynecological cancers has been reported (4,5). Our case was diagnosed with breast, ovarian and endometrial primary malignancies.

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 (1). Another suggestion says that the extended Müllerian system, comprising the ovarian epithelium, fallopian tube, uterine corpus, and cervix, may respond as a single morphologic unit to produce primary carcinomas in multiple sites (6). Others suggest that these neoplasms originate in metaplasia occurring in histologically similar epithelium of the genital tract and peritoneum (7). Soliman et al. found that young age, obesity, premenopausal status, and nulliparity were the distinct clinical characteristics of the women with synchronous primary cancers of the endometrium and ovary, and authors suggested that a hormonal field effect might account for the development of the simultaneous endometrioid cancers (8). But in contrast to the literature, our case was advanced age, postmenopausal status and multiparous.

In the literature, some authors published that women with previous breast cancer had an elevated risk of developing a second primary gynecologic cancer compared with the general population (9). Arpacı et al. found that the gynecologic cancers were the most common cancers among women suffered from breast cancer (3). They suggested that radiotherapy or chemotherapy

which the patients have received for their first cancer could play an important role in the development of multiple primary malignancies. In our case, the process is similar to the literature. On the other hand, the granulosa cell tumors are hormonally active tumors and these tumors produce estradiol (10). In our case, 80% consisting of estrogen receptor positivity in breast and the estrogen secreted from ovarian tumor may have been effective in the progression of breast cancer.

Synchronous cancers in the endometrium and ovary of female genital tract are rare, but well-recognized events (6). The most common ovarian histology, in series including synchronous primary neoplasias of the endometrium and ovary is endometrioid type (8). In contrast to literature, the ovarian histology of our case was adult type granulosa cell tumor and the endometrial histology was serous adenocarcinoma.

The association of endometrial and ovarian cancer can be divided into 3 groups: 1) ovarian metastasis of endometrial cancer, 2) endometrial metastasis of ovarian cancer, 3) Synchronous primary cancers of the endometrium and ovary (9). The distinction between dual primary cancer and metastatic lesion from one primary cancer is relatively easy when histologies of the two cancers are different from one another. When both tumors share the same histologic features, it may be difficult to distinguish between metastatic and independent malignancies (11). In our case, the endometrial cancer type was serous adenocarcinoma and the ovarian tumor type was adult type granulosa cell tumor. These different histologic types of tumors support synchronous primary cancers diagnosis.

It is important to distinguish multiple primaries from metastatic lesions because they carry a different prognosis. The criteria of identification of the synchronous primary cancers include either different histologic types (major criterion) or all of the following minor criteria: both tumors confined to primary sites, no direct extension between tumors, and no lymphovascular tumor emboli, no or only superficial invasion and distant metastasis (6).

When compared with patients having metastatic lesions, synchronous primary cancer had a much better survival rates than a metastatic case due to the detection of patients at earlier clinical stage and lower grade (1). It is known that the endometrial cancer usually produces earlier symptoms, thus diagnosed at early stage. But our case did not present any symptoms that lead to early diagnosis and the endometrial cancer stage of our case was FIGO stage IIIB. This stage includes the vaginal and/or parametrial involvement (12). It is known that the survival rates of stage III tumors are 45% (13). Based on histopathology endometrial cancer type of our case was type II. Type II endometrial cancers are not hormone dependent and they have p53 mutations and loss of heterozygosity at several chromosomal loci. They are associated with early spread and worse prognosis (13).

Patients with simultaneous endometrial cancer and ovarian cancer have a significantly better prognosis than patients with advanced endometrial cancer and ovarian metastasis. Also, synchronous primaries show better survival rates than single aggressive ovarian cancers (14). Surgical treatment alone may be enough for early stage patients. Chemotherapy plus radiotherapy may be necessary for advanced stage patients (15). Due to the stage of our case, surgery was followed by pelvic RT and chemotherapy. In the follow-up the megestrol acetate was added to therapy. Unfortunately, our case has poor prognosis with advanced stage and she died 22 months after diagnosis.

Authors have no disclosure

REFERENCES

1. Güzin K, Tekcan C, Naki MM, Kayataş S, Zemheri E, Kanadikirik F, et al. Synchronous primary cancers of the endometrium and ovary: a case report. *Eur J Gynaecol Oncol.* 2006;27(4):425-8.
2. Escobar PA, Smith MT, Vasishta A, Hubbard AE, Zhang L. Leukemia-specific chromosome damage detected by comet with florescence in situ hybridization (comet-FISH). *Mutagenesis.* 2007;22, 321-7.
3. Arpacı E, Tokluoglu S, Yetigyigit T, Alkis N. Multiple primary malignancies-a retrospective analysis at a single center in Turkey. *Asian Pac J Cancer Prev.* 2013;14(2):769-73.
4. Phupong V, Khemapech N, Triratanachat S. Triple synchronous primary cervical, endometrial and ovarian cancer with four different histologic patterns. *Arch Gynecol Obstet.* 2007;276:655-658.
5. Atasever M, Yilmaz B, Dilek G, Akçay EY, Kelekeci S. Synchronous Primary Carcinoma in 5 Different Organs of a Female Genital Tract An Unusual Case and Review of the Literature. *Int J of Gynecol Cancer.* 2009;19:802-7.
6. Eifel P, Hendrickson M, Ross J, Ballon S, Martinez A, Kempson R. Simultaneous presentation of carcinoma involving the ovary and the uterine corpus. *Cancer* 1982;50:163-70.
7. Ayhan A, Yalçın OT, Tuncer ZS, Gürgan T, Küçükali T. Synchronous primary malignancies of the female genital tract *Eur J Obstet Gynecol Reprod Biol.* 1992; 45:63-6.
8. Soliman PT, Slomovitz BM, Broaddus RR, Sun CC, Oh JC, Eifel PJ, et al. Synchronous primary cancers of the endometrium and ovary: a single institution review of 84 cases [review]. *Gynecol Oncol.* 2004;94:456-62.
9. Gülhan I, Eser S, Yakut C, Bige O, İlhan E, Yildirim Y, et al. Second primary gynecologic cancers after breast cancer in Turkish women. *Int J Gynecol Cancer,* 2009;19:648-50.
10. Busquets M, Gonzalez-Bosquet E, Muchart J, Rovira C, Laïlla JM. Granulosa cell tumor and endometrial cancer: a case report and review of the literature. *Eur J Gynaecol Oncol.* 2010;31(5):575-8.
11. Prat J, Matias-Guiu X, Barreto J. Simultaneous carcinoma involving the endometrium and ovary: a clinicopathologic, immunohistochemical, and DNA flow cytometric study of 18 cases. *Cancer* 1991;68:2455-9.
12. Lewin S, Herzog T, Barrena Medel NI, Deutsch I, Burke WM, Sun X, et al. Comparative performance of the new versus old FIGO staging system for endometrial cancer. *Obstet Gynecol.* 2010; 116: 1141-9.
13. Plataniotis G, Castiglione M. Endometrial cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol.* 2010; 21:41-5.
14. Juhasz-Böss, Fehm T, Becker S, Rothmund R, Krämer B, Staebler A. Endometrial Cancer: Comparison of Patients with Synchronous Primary Carcinoma of the Endometrium and Ovary vs. Endometrial Carcinoma with Ovarian Metastases. *Geburtshilfe Frauenheilkd.* 2012 Aug;72(8): 721-726.
15. Ma SK, Zhang HT, Sun YC, Wu LY. Synchronous primary cancers of the endometrium and ovary: review of 43 cases. *Zhonghua Zhong Liu Za Zhi.* 2008 Sep;30(9):690-4.