RESEARCH COMMUNICATION

Synchronous Primary Cancers of the Female Reproductive Tract in Turkish Women

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Abstract

Objectives: To evaluate the synchronous gynecologic cancers in Turkish women. Materials and methods: A population-based longitudinal cohort study was conducted using Izmir Cancer Registry (ICR) data on gynecologic cancer patients diagnosed in the period 1993 to 2005. The registry covers the 3.7 million population of Izmir and has been collecting data on cancer incidence and survival of cancer patients' since 1992. The ICR collects data on all new cases of cancer from all the hospitals (n = 22) in the city. Results: A total of 4,185 women were identified with gynecologic cancer between 1993 and 2005, 1,526 with endometrial, 1,206 with cervical, 1,198 with ovarian, 115 with vulvar, 67 with other uterine (sarcoma etc.), 33 with vaginal and 40 with other gynecologic cancers (tuba uterina etc.). Fifty-five (1.3%) patients with invasive synchronous primary cancers were identified, 43 of these tumor pairs being endometrium-ovaries (81%), 66 of all lesions being endometrioid adenocarcinomas. Conclusions: Independent primary tumors of the endometrium and ovary are the most commonly encountered synchronous tumors of the female genital tractus with endometrioid adenocarcinoma as the most frequent component.

Keywords: Synchronous gynecologic cancers - Turkish women

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Introduction

Although there is no consensus on the definition of synchronous cancer, commonly two or more primary tumors that occur in a patient closely in time are termed as synchronous tumors (Woodruff et al., 1985). Synchronous tumors may arise in the same site or different sites with different morphologies or in the different sites with the same morphology. The occurrence of synchronous primary cancers of the genital tract is rare and the occurrence rate differs between 0.7 and 1.8% in patients with gynecologic tumors (Eisner et al., 1989).

The accurate diagnosis of synchronous primary gynecological tumors is important because a diagnosis of synchronous cancer would affect the treatment (Chiang et al., 2008). Independent primary tumors of the endometrium and ovary were stated as the most commonly encountered synchronous tumors of the female genital tractus, occurring in approximately 10% of all women with ovarian tumors and 5% of all women with endometrial tumors by the plenty of studies (Soliman et al., 2004; Lou et al., 2006; Zaino et al., 2001).

In this study we aimed to evaluate the frequency and types of synchronous gynecologic cancers in Turkish women.

Materials and Methods

A population-based longitudinal cohort study was conducted using the Izmir Cancer Registry (ICR) data on gynecologic cancer patients diagnosed in the period 1993 to 2005. The registry covers the 3.7 million population of Izmir and has been collecting data on cancer incidence and survival of cancer patients' since 1992. The ICR collects data on all new cases of cancer from all the hospitals (n = 22) in the province. Izmir Cancer Registry Center has been used International Classification of Diseases: Oncology (ICD-O3) for coding of the neoplasms and follow IACR and ENCR rules for distinction of the multiple primaries (Curado et al., 2007; Eser, 2007).

Results

A total of 29678 women with cancer and 4185 women with gynecologic cancer were identified between 1993 and 2005. Of the 4185 patients, 1526 had endometrial, 1206 had cervical, 1198 had ovarian, 115 had vulvar, 67 had other uterin cancers (sarcoma etc.), 33 had vaginal

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Table 1. Histopathological Subtypes and Sites of Syncronous Cancers

	Endo	Ovary	Cervix	Vag	Vul	Tuba	Total
Endometrioid AC	36	29				1	66
Clear cell 5	5	6	2				13
Papillary serous AC	2	7	2				11
Mucinous carcinoma	2	3					5
Squomous cell	2		1		1		4
Adenosquomous	2		2	2			6
MM mullerian tumor	3						3
Granulosa cell		1					1
MM mesodermal tumor		1					1
Total	52	47	7	2	1	1	110

Endo, endometrium; Vag, vagina; Vul, vulva; AC, adenocarcinoma; MM, malignant mixed

cancers, 40 had other gynecologic cancers (tuba uterina etc.).

Fifty-five (1.3%) patients with invasive synchronous primary cancers were identified among 4185 patients. The median age at diagnosis was 53.2 (33-76) years. 43 of 55 tumor pairs were the pair of endometrium-ovaries (81%), 4 endometrium-cervix, 2 endometrium-vagina,1 endometrium- vulva, 1 endometrium-endometrium, 1 cervix-cervix, 1 ovary- ovary, 1 ovary-tuba, 1 ovary-cervix. Histological type of 66/110 (60%) cancers were the endometrioid adenocarcinoma. Table 1 shows the histological subtypes and the sites of synchronous cancers. The median age at diagnosis of women with endometrial and ovarian cancer was 53.6 (33-76) years.

Discussion

Of the 4185 women 55 had synchronous gynecologic cancers (%1.3). The most frequent synchronous genital lesions were ovarian and endometrial cancers in 43 patients (81%). The most frequent cancer type was the endometrioid adenocarcinoma (66/110, 60%).

In our study, the median age at diagnosis of women with synchronous endometrial and ovarian cancer was 52.6 (33-76) years in contrast, women who develop endometrial or ovarian cancer alone are predominantly postmenopausal, the median diagnosis age was between 60–63 years (Soliman et al., 2004; Lou et al., 2006; Zaino et al. 2001,Young et al. 2002, Brown et al. 2001). Other studies also reported that, patients having synchronous cancers were younger than their counterparts (Williams et al., 2009). This indicates a positive prognostic criterion. Definition of synchronous cancers could not reach a consensus and the cancers which are diagnosed within different periods might be evaluated as synchronous cancers. In our study, the cancers which were simultaneously diagnosed were accepted as synchronous cancers.

One of the important problems about the synchronous cancers is the difficulty of differential diagnosis of the simultaneous cancers, it they are primary or metastatic. Despite the fact that there are not available precise criteria about the issue, there are some approaches in pathological aspect. For example if both of the simultaneous ovarian and endometrium tumors are endometrioid type, they are mostly independent primary tumors and prognosis is better (Eifel et al., 1982). For clear cell or serous tumors, the prognosis are worse and the tumor which is bigger and has an advanced stage has metastatic spread to the other site. Metastasis from endometrium to over is in question in case of the simultenous tumors of mixt mullerien and grade III endometrioid tumors (Krigman et al., 1995). If the size of the ovarian tumor is less than 5 cm and bilateral; and endometrioid tumor has deep invasion and has two or more of the findings such as lymphvascular tumor thrombosis or tubular invasion, there is metastasis from endometrium to ovarium on the carpet (Culton et al., 2006). On the other hand, the presences of the concomitant atypical endometrial hyperplasia, the superficial ovary tumors with multiple foci support the ovarial metastasis of primary endometrial tumor. If a large tumor developed in the center of the ovary; has invasion from seroza to myometrium and invaded the peritoneal surfaces, then the primary focus is ovary. In the case of squamous cell type simultaneous cervical and ovarian tumors, ovarian metastasis from primary cervical cancer might be thought. On the other hand if there are simultaneous adenocarcinomas of cervix and ovarium, the deepness of the cervical invasion and invasion to the extraserosa support primary cervical tumor. Despite all of those information, sometimes the precise distinction cannot be made (Zaino et al., 2001).

Our findings are consistent with the literature on synchronous gynecologic cancer proportion and cancer types. Eisner et al. found that the ratio of primary synchronous cancers was 0.7% in their study that was conducted on 3863 cancer patients (Eisner et al., 1989). In this study, the most frequent synchronous gynecological cancers was found as low stage and low grade ovarian and endometrial cancers. Similarly, Ayhan et al. found that low stage and low grade ovarian and endometrial cancers were the most frequent synchronous primary genital tumors (51.7%) and 1.7% of the tumors were synchronous (Ayhan et al., 1992). They also reported 73.3% 5-year survival rate for the patient with the synchronous ovarian and endometrial cancers. Gungor et al. reported that ovarian and endometrial synchronous cancers were the most frequent synchronous cancers and had 77% survival rate in 21 patients with synchronous gynecological cancers (Gungor et al., 2009).

Zaino et al. retrospectively evaluated 74 patients who had ovarian and endometrial cancers and found that 86% of the patients had endometriod carcinoma (Zaino et al.,2001).

Caduff et all reported that endometrioid tumors of the ovary and endometrium, although histologically similar, may arise from different genetic events, whereas uterine papillary serous carcinoma shares with its ovarian counterpart several molecular alterations that may account for its aggressive clinical behavior (Caduff et al., 1998).

Synchronous ovarian and endometrial cancers are the most studied synchronous gynecological cancers. We found 1.0% (43/4185) of the gynecological cancers were synchronous ovarian and endometrial cancers. Some studies reported 10% of the ovarian cancer patients had endometrial cancer also (Soliman et al. 2004, Lou et al. 2006, Zaino et al. 2001).

However, in a large population-based study, Williams et al. found that proportion of synchronous ovarian and endometrial cancers changed in a range from 1.7% to 2.4% of all ovarian cancer cases depend to the interval between first and second cancer (Williams et al., 2009). They used the Surveillance, Epidemiology, and End Results Program's definition (SEER) for synchronous cancers, as cancers of the endometrium and ovary diagnosed within 2 months of each other in this study. They concluded that, the discrepancy in the estimate of these synchronous cancers might be a result of differences in study population in the different studies, because most studies reporting higher frequencies of synchronous cancers were hospital-based with fewer than 100 patients. Secondly, prior studies have used various criteria to distinguish between synchronous primary cancers and a single primary cancer with metastasis. Van Niekerk et al. using the Netherlands Cancer Registry, found that uterine or endometrial cancers detected within the same year of ovarian cancer diagnosis accounted for 2.6% of the 5,366 patients diagnosed with ovarian cancer (van Niekerk et al., 2007).

According to Williams's study it is found that synchronous ovarian and endometrial cancers exhibit favorable survival outcomes as compared with single primary ovarian cancers. They explained this event by favorable characteristics associated with synchronous tumors, including younger age at diagnosis, earlier stage of disease, and better grade of disease.

Synchronous cancers, as well as in different sites, may also develop in the same site. We found three cancer pairs which developed in endometrium, ovarium and cervix like that. There were endomedrioid and clear cell carcinomas in endometrium; adenocarcinoma and squamous cell carcinoma in cervix; and endometrioid carcinoma and mixef mesodermal carcinoma in ovarium.

In conclusion independent primary tumors of the endometrium and ovary are the most commonly encountered synchronous tumors of the female genital tractus and endometrioid adenocarcinoma is the most frequent cancer in synchronous gynecologic tumors in Turkish women.

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