Synchronous primary neoplasms of the uterine corpus and the ovary: a case report

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Summary

Objective: To determine the frequency of synchronous primary neoplasia of the ovaries in patients with primary malignant neoplasia of the uterus, and to analyze the clinical and histological characteristics of these cases.

Materials and Methods: Clinicopathological data from a series of patients treated for primary malignant neoplasia of the uterus between 1985 and November 2003 have been studied retrospectively.

Results: Synchronous primary neoplasia of the ovaries was found in 13 out of 173 patients (7.5%) treated for primary malignant neoplasia of the uterus. In four patients (2.3%) the histological findings suggested ovarian metastases from primary endometrial adenocarcinoma. In four other cases (2.3%) there was extension of the primary uterine sarcoma to the ovaries. In the remaining five cases (2.9%) primary endometrial adenocarcinoma coexisted with: a) ovarian cystadenocarcinoma in two cases, b) ovarian fibroma-thecoma in two cases, and c) ovarian tumor of borderline malignancy in one case.

Conclusions: Coexistence of distinct primary neoplasias in the uterus and ovaries is rare. Diagnosis of two primary malignancies in the uterus and ovaries should be based on histological examination. Treatment should be appropriate for both tumors, taking into consideration that treatment of one tumor will not lead to subtreatment of the other.

Key words: Synchronous primary neoplasia; Uterus; Ovaries; Diagnosis; Treatment.

Introduction

Synchronous primary tumors of the female genital tract are relatively rare, comprising only 1% to 6% of all genital neoplasms. Synchronous primary neoplasms of the ovary in patients with primary endometrial carcinoma are the most frequent combination of multiple primary neoplasms of the female genital tract, with a frequency ranging between 2 and 8.5% in different series [1, 2].

The etiopathogenesis of synchronous primary tumors of the endometrium and ovary remains unclear and several theories have been proposed. The term "extended müllerian system" has been used to describe the ovarian surface, fallopian tubes, cervix and the endometrium since they all have the same embryologic derivation from the müllerian duct and respond in some circumstances as a morphological unit. For example, during pregnancy the stroma of the cervix, fallopian tube, and ovary may exhibit a decidual reaction identical to that of the endometrium. Moreover, histologically similar or identical proliferations develop occasionally in more than one anatomic component of the system [3]. Based on these observations, it has been hypothesized that a given carcinogenic stimulus may produce similar epithelial proliferations in both the ovary and the endometrium [2, 4-6]. Alternatively, others have suggested that these neoplasms represent metaplasia occurring in the epithelium of the genital tract and the histologically similar peritoneum [2, 7]. In addition, it is quite likely that estrogens are important in synchronous endometrial and ovarian neoplasias [2].

The presence of different tumors in both the uterus and ovary lead to a number of diagnostic and therapeutic questions. Concerning diagnosis: Are there two distinct primary neoplasms, one in each organ, or only one primary tumor of one organ spreading to the other? Which diagnostic criteria should be used in order to differentiate synchronous primary neoplasms from the spread of a sole primary neoplasm? What is the optimal therapeutic strategy in such cases?

Material and Methods

Clinicopathological data from 194 consecutive patients with primary malignancies of the uterine corpus were studied retrospectively. All patients were treated in our department between 1985 and 2003.

The major criterion for characterizing ovarian tumors in patients with primary malignancies of the uterine corpus as synchronous primary neoplasias was different histology. In addition, the following characteristics were present in all cases: a) both tumors were each confined to one organ, one in the ovary and one in the uterus, b) there was no direct extension from one tumor to the other, c) there were no malignant cell emboli in the lymph and blood vessels, and d) there were no distant metastases.

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Results

Twenty-one out of 194 patients with primary malignancy of the uterine corpus were excluded from the study due to inadequate data. Synchronous neoplasia in the ovaries was found in 13 out of the remaining 173 patients (7.5%): 1) In four patients (2.3%) histopathological examination suggested metastases of primary endometrial adenocarcinoma to the ovaries. 2) In four other cases (2.3%), there was extension of primary uterine sarcoma to the ovaries. 3) In the remaining five cases (2.9%) primary endometrial adenocarcinoma coexisted with a) ovarian cystadenocarcinoma in two cases, b) ovarian fibroma-thecoma in two cases, and c) borderline ovarian tumor in one case.

Clinicopathological data from the five patients with two synchronous primary neoplasias of the endometrium and ovaries are summarized in Table 1. The mean patient age was 66.4 years, ranging between 53 and 75 years. All five patients had endometrial adenocarcinoma, FIGO Stage I, histological grade 1-2. The two patients with synchronous malignant ovarian neoplasia had ovarian cystadenocarcinoma, FIGO Stage IC, histological grade 1.

All five patients with synchronous neoplasias of the endometrium and ovaries were treated with total abdominal hysterectomy and bilateral salpingo-oophorectomy. Typical staging with omentectomy and peritoneal biopsies was done in one patient with macroscopically evident ovarian malignancy. All five patients received progestin therapy postoperatively. The patient with endometrial adenocarcinoma FIGO Stage IC underwent postoperative radiotherapy. One of the two patients with ovarian carcinoma FIGO Stage IC received postoperative chemotherapy while the other refused to do so.

Table 1. — *Clinicopathological data of patients with synchronous primary neoplasms of the uterine corpus and ovary*

Patient	Age	Endometrial adenocarcinoma	Ovarian neoplasia
TD	61	Stage IB-G1	Stage IC-G1 cystadenocarcinoma
KM	72	Stage IA-G1	Stage IC-G1 cystadenocarcinoma
TA	53	Stage IB-G1	Stage IA-borderline malignancy
TM	71	Stage IC-G2	Stage IA-fibroma-thecoma
GM	75	Stage IA-G1	Stage IA-fibroma-thecoma

G: histological grading.

Discussion

Coexistence of two distinct primary neoplasias in the uterine corpus and the ovaries was relatively rare in the present study. In all cases with synchronous primary neoplasias, endometrial carcinoma coexisted with a malignant or benign ovarian tumor. The frequency of this combination was 2.9% which is consistent with results from previously published series in which frequency ranged between 2 and 8.5% [1, 2].

The identification of synchronous ovarian malignancies in women with endometrial carcinoma is complicated by the fact that the ovary represents a possible site of metastatic spread from the endometrium. Most likely patients with synchronous tumors are those with tumors of different histology [1]. Interestingly, these women comprise only a minority of patients included in published series of synchronous primaries [1-5, 8-15]. Many and in some cases all of the women included in these reports may simply have had ovarian metastases from uterine primary tumors [1]. Besides the major criterion of different histology of endometrial and ovarian tumors, other minor criteria have been used [3, 8, 9]: a) both tumors confined to primary sites, b) no direct extension between the two tumors, c) no lymphovascular tumor emboli, d) no or only superficial myometrial invasion, and e) no distant metastases. Molecular methods have been used in order to distinguish metastatic from independent primary tumors, but the differential diagnosis must still largely rely on conventional clinicopathological criteria [4, 9, 16-18].

All patients in our series with synchronous primary neoplasias of the endometrium and ovaries were older than 60 years. This is consistent with the findings of a previous study [1], in which the major criterion of different histology was also used. In contrast, the mean age was lower in earlier reports [2, 3, 8-15]. The reason for this discrepancy is probably due to the fact that different criteria were used in these reports, which included tumors with similar histology. It should also be noted that in a previous study [19] the prevalence of second primary ovarian tumors in patients younger than 45 years was five times more compared with that of older women. However, age was not found to be an independent risk factor for the development of a synchronous ovarian malignancy [19, 20].

Though the number of patients with synchronous primary neoplasias of the endometrium and ovaries in our series was relatively low, it seems that the most usual histopathological types of primary ovarian neoplasia were cystadenocarcinoma and fibroma-thecoma. In previously reported series the most common histological type of ovarian malignancy was endometrioid tumor, but tumors of similar histology were also included in these reports [1]. Concerning malignant neoplasias, our findings are in agreement with those of a previous study [1] in which the most frequent ovarian histologies were mucinous and serous cystadenocarcinomas. We also found two cases of ovarian fibroma-thecoma which, as previously reported [19], may have been related to the endometrial carcinoma on the basis of hormone secretion.

We also detected one case of endometrial carcinoma with a synchronous ovarian tumor of borderline malignancy. In contrast to prior reports, Castro *et al.* [1] also reported four cases of borderline ovarian malignancies in their series. In a review of 94 borderline ovarian tumors, concomitant endometrial carcinoma was noted in 3.2% of the patients [1, 20]. We did not find any case of ovarian granulosa cell tumor in patients with primary malignancies of the uterine corpus. In previous studies only three cases of granulosa cell tumors of the ovaries have been reported [1, 2]. This was surprising given the known

association between granulosa cell tumors and endometrial cancer, as reported in a review of 198 granulosa cell ovarian tumors in which endometrial carcinoma was reported in 6% of the patients [1, 21].

Patients with synchronous primary tumors of the endometrium and ovaries seem to constitute a quite different prognostic entity, with a more favorable outcome than single advanced-stage cancer at either site [9], with survival rates ranging between 73.3% and 100% in previous reports [1-3, 10, 14, 15]. Even in studies in which tumors of similar histology were also included, prognosis was favorable [22]. Endometrial cancer usually produces symptoms earlier, and thus ovarian cancer may be detected at an earlier stage if it coexists with a synchronous primary endometrial tumor [9].

The risk of occult malignant disease in the ovaries either from a synchronous primary ovarian malignancy or from metastases is not zero, making total abdominal hysterectomy with bilateral salpingo-oophorectomy necessary in cases of endometrial cancer. In younger patients unilateral oophorectomy at the time of hysterectomy for endometrial carcinoma may be considered if only one ovary is enlarged and if frozen-section examination of that ovary reveals a thecoma [19]. No definitive treatment guidelines exist given the small number of reported cases and the variety of treatments used so far. However, the excellent outcome in low-stage, low-grade tumors treated with surgery alone supports this approach, while patients with more advanced disease stage, unfavorable histologies, and high-grade disease should receive treatment for both tumors [1]. In any case, it is imperative that treatment of one tumor does not compromise the treatment of the other [1].

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