

CLINICOPATHOLOGICAL CHARACTERISTICS OF PATIENTS WITH SYNCHRONOUS PRIMARY OVARIAN AND ENDOMETRIAL CANCERS

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Abstract

Purpose: Synchronous primary endometrial and ovarian cancers are infrequent. The objective of this study is to evaluate clinicopathological characteristics of synchronous endometrial and ovarian cancers treated in our institution.

Materials and Methods: The clinicopathological characteristics of 12 patients with synchronous ovarian and endometrial cancers treated at Shaukat Khanum Memorial Cancer Hospital and Research Centre, Lahore, Pakistan, from July 2005 to July 2015, were reviewed retrospectively in depth from hospital database. The WHO committee classification was used for the histologic determination and staged based on International Federation of Gynaecology and Obstetrics (FIGO) staging.

Results: The median age at the time of diagnosis was 50 years (range 23–66 years). The incidence of synchronous primary endometrial and ovarian cancers was 2.01% in patients with endometrial cancer. A total of seven patients were menopausal (58%) and eight patients were nulliparous (66%); the median body mass index (BMI) was 29 kg/m² (range, 20–38). Abnormal uterine bleeding was the most common presenting symptom. According to FIGO stage, 10 cases of endometrial were Stage I/II (84%) and two cases were Stage III (16%). Of the ovarian cancers, nine cases were Stage I/II (83.3%) and two cases were Stage III (16.7%). Endometrial cancer was the main pathological type in uterine carcinoma (86%) followed by serous carcinoma (14%), and similarly, for ovarian cancer, endometrial was the most common pathology (67%) followed by serous/clear cell (16%) and mucinous (16.7%). Most endometrial and ovarian primaries in our series were Grade I and II tumours, 83% and 66%, respectively. 8 patients (66%) had similar histology in both primaries. All patients underwent surgical intervention. Only one patient did not receive any post-operative adjuvant therapy. 10 patients received platinum-based adjuvant chemotherapy and six patients received adjuvant radiotherapy.

Conclusion: Synchronous primary endometrial and ovarian cancers are infrequent and distinct set of patients. Abnormal per vaginal bleed was the most common symptom which helped in early detection. Majority of the patients belong to concordant endometrial histology, low grade, had younger age and high BMI. Treatment should be tailored to the stage, histology and grade of the individual tumours.

Key words: Endometrial cancer, ovarian cancer, synchronous tumours

Introduction

Synchronous primary tumours of the endometrium and ovary are relatively uncommon, representing the most common combination of synchronous primary cancer of the female genital tract.^[1-3] Approximately 5% of all

patients with endometrial cancer appear to have ovarian cancer synchronously and 10% other way around.^[4]

The pathogenesis remains unclear. According to the theory of a secondary Mullerian system, epithelium of cervix, uterus, fallopian tubes, ovaries and peritoneal surface has shared molecular receptors responding to carcinogenic stimulus, leading to the development of multiple primary malignancies synchronously.^[5,6] However, no absolute specific criteria exist to determine whether they represent

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metastasis, independent primary tumours or dysplastic process involving the Mullerian epithelium.

Patients with synchronous primary endometrial and ovarian cancers have distinct clinical characteristics including young age, obesity, premenopausal status and nulliparity.^[7] The aim of the present retrospective study is to evaluate the clinicopathological characteristics of synchronous endometrial and ovarian cancer treated in our institution.

Materials and Methods

From July 2005 to July 2015, the hospital tumour registry and information systems identified 12 patients with synchronous ovarian and endometrial cancer. Electronic and archived medical records were accessed to obtain clinicopathological data including age at diagnosis, presenting symptoms, body mass index (BMI), parity, treatment, histological subtypes and stage of disease.

Of these 12 patients, eight patients presented with per vaginal bleeding and were diagnosed with primary uterine carcinoma on endometrial curetting. These patients underwent upfront total hysterectomy and bilateral salpingo-oophorectomy, whereas four patients underwent upfront total hysterectomy, bilateral salpingo-oophorectomy, pelvic lymphadenectomy, omentectomy and peritoneal washings for suspected ovarian primary. The surgical specimens were reviewed by our pathologists and the diagnosis of synchronous malignancies was made according to the criteria by Scully *et al.*^[8] All patients had incidental finding of synchronous second primary on surgical specimens.

Adjuvant therapy was proposed for selected patients based on an evaluation of the risk factors for the two synchronous carcinomas such as stage, grade, histology and accuracy of surgical staging.

Patients were considered at low risk, if they had endometrial cancer Stage IA Grade 1–2 and/or ovarian cancer Stage IA–B Grade 1; at intermediate risk, if they had endometrial cancer Stage IA Grade 3 and Stage IB Grade 1–2, and/or ovarian cancer Stage IA–B Grade 2 and at high risk, if they had endometrial cancer Stage IB Grade 3, Stage IIB and clear cell or serous carcinoma, and/or ovarian cancer Stage IC or any Grade 3. The risk of Stage IIA endometrial cancers was defined according to grade and depth of myometrium invasion.

Adjuvant chemotherapy was given to patients with intermediate and high-risk ovarian cancer.

Whereas adjuvant vaginal brachytherapy was given to intermediate or high-risk Stage I endometrial carcinomas, external beam radiotherapy along with vaginal brachytherapy was given to Stage II endometrial carcinoma.

Follow-up examinations were conducted every 3–4 months during the first 2 years, every 6 months during next 3 years and then once a year.

Results

The median age of the 12 patients was 50 years (range 23–66 years). Four of the patients were aged <50, whereas eight patients were aged >50. The median BMI was 29 kg/m² (range 20–38), 8 (67%) of the 12 patients were obese (BMI >28). A total of seven patients were menopausal (58%) and eight patients were nulliparous (66%). The most common presenting symptom was abnormal uterine bleeding occurring in 6 patients (50%), abdominal pain and abdominal fullness in 5 patients (42%) and only one case exhibited vaginal discharge [Table 1].

Of the 12 patients, eight had hysterectomy and bilateral salpingo-oophorectomy and the remaining four patients had total hysterectomy, bilateral salpingo-oophorectomy, omentectomy with appendectomy and pelvic lymph node dissection.

The histopathological characteristics of the endometrial cancers are listed in Table 2. We found that 50% of patient had Grade I tumours and 42% had International Federation of Gynaecology and Obstetrics (FIGO) Stage I cancers. Myometrium invasion was seen in 50% of patients and lymphovascular space invasion was not found in any patient.

The histopathological characteristics of the ovarian cancer are listed in Table 3. We found that 42% had FIGO Stage I cancers and 50% had Grade I cancers. Endometrial cancer was the main pathological type in uterine carcinoma (86%) followed by serous carcinoma (14%), and similarly, for ovarian cancer, endometrial was the most common pathology (67%) followed by serous/clear cell (16%) and mucinous (16.7%).

Concordant endometrial/endometrial histology was seen in 68% (8/12), endometrial/mucinous in 16% (2/12),

Table 1: Patient characteristics

Patient characteristics	Number (%)
Age	
<50	4 (23)
>50	8 (67)
Pre-menopausal	6 (50)
Postmenopausal	6 (50)
Comorbid conditions	
Diabetes	3 (25)
Hypertension	4 (33)
Presenting symptoms	
Abnormal bleeding	6 (50)
Abdominal/pelvic mass	0
Abdominal distension	3 (25)
Abdominal/pelvic pain	2 (17)
Others	1 (8)

Table 2: Tumour characteristics endometrial cancer

Characteristics	Frequency number (%)
Stage	
IA	5 (42)
IB	4 (33)
II	2 (17)
III	1 (8)
Myometrium invasion	
<50%	6 (50)
>50%	6 (50)
Grade	
I	6 (50)
II	4 (33)
III	2 (17)
Histology	
Endometrial	10 (86)
Serous	2 (14)
Adjuvant radiotherapy	
Vaginal brachytherapy	5 (42)
External pelvic and vaginal brachytherapy	1 (8)
None	6 (50)

endometrial/serous in 8% (1/12) and endometrial/mucinous in 8% (1/12) of patients.

A total of 10 patients received platinum-based adjuvant chemotherapy, five patients received both chemotherapy

and radiotherapy and one patient received radiotherapy alone.

Discussion

The results of our study reflect the interesting data about the biological behaviour of synchronous endometrial and ovarian carcinomas. Reported incidence rates in literature range from 2% to 10%;^[7-12] however it is 2.01% of all early-stage endometrial cancers treated at our institution.

The median age at diagnosis was 50 years. The previous studies have also reported a younger median age in patients with synchronous endometrial and ovarian cancers. It is worth mentioning, 3 women (25%) were under 40 years of age at the time of diagnosis. These data support previous reports about the development risk of coexisting cancer and the common presentation of synchronous cancer in premenopausal or women of reproductive age.^[2,13,14]

Obesity is well-known risk factor for the development of endometrial cancer. Soliman *et al.* reported that 35% of patients were obese with BMI >30.^[7] In the study by Nishimura *et al.*, the mean BMI of Japanese females with synchronous primary endometrial and ovarian cancers was 22.6 ± 3.4 kg/m², but the authors did not report the obesity rates.^[15] In the present study, the median BMI was 29 kg/m² (range 20–38), 8 (67%) of the 12 patients were obese (BMI >28).

The most common histology of synchronous ovarian and endometrial tumour is endometrial type.^[7,13,16] In the present study, 86% of endometrial cancers and 67% of ovarian cancers were endometrial. We experienced that only 17% of endometrial and 25% of ovarian were poorly differentiated which was concordant with a 30% incidence typically detected in Stage I ovarian cancer. The incidence of myometrium invasion was 50% and there was no incidence of vascular invasion.

According to literature, most patients with synchronous cancers present with symptoms characteristic of endometrial cancer. Abnormal uterine bleeding and abdominal pain were the main presenting symptoms.

In our series, median follow-up was 9 months (range: 4–41 months). Three patients experienced relapse. Other

Table 3: Tumour characteristics ovarian cancer

Characteristics	Frequency number (%)
Stage	
IA	5 (42)
IB	3 (25)
IC	2 (17)
IIIA	2 (16)
Grade	
I	6 (50)
II	2 (17)
III	3 (25)
Unknown	1 (8)
Histology	
Endometrial	8 (67)
Clear	1 (8)
Serous	1 (8)
Mucinous	2 (17)
Adjuvant chemotherapy	
Yes	10 (84)
No	2 (16)

patients are alive without relapse. Given the small number of patients, no overall or disease-free survival data could be ascertained.

Our study was conducted in a single institution rather than multicentre analysis. The major limitation of the study was limited number and retrospective review. The diagnosis of synchronous malignancy was confirmed only after pathologic examinations, and it was hard to predict before surgical staging.

Guidelines for adjuvant treatment in patients with synchronous cancers have not been yet established. It is not possible to make definitive conclusion on optimal treatment. The excellent outcome in low-stage, low-grade tumours treated with surgery alone, however, supports the merits of this approach. Patients with more advanced stage, unfavourable histologies and high-grade disease should receive treatment tailored to both tumours.

Conclusion

The incidence of synchronous endometrial and ovarian cancer is remarkable, especially in premenopausal or young woman of reproductive age. Synchronous carcinomas show very favourable pathological features compared with the general

endometrial or ovarian cancers. Treatment should be tailored to the histology, stage and grade of the individual tumours.

Conflict of Interest

The authors declare that they have no conflict of interest.

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