Journal of Pathology of Nepal (2012) Vol. **2**, 189 - 192

Journal of
PATHOLOGY
of Nepal
www.acpnepal.com

Original Article

Synchronous primary tumors of the endometrium and ovary

Karki S[1], Chapagain U[1]

[1]*Department of pathology, Tribhuvan University Teaching Hospital, Kathmandu, Nepal*

Keywords:

Endometrial cancer;
Ovarian cancer;
Synchronous primary neoplasm

ABSTRACT

Background: Primary synchronous cancer of the female genital tract is a relatively uncommon. Simultaneously detected endometrial and ovarian malignancies constitute the commonest occurrence. A set of pathological criteria has been described to differentiate synchronous primaries from metastatic tumors. The purpose of this study was to characterize patients with synchronous primary endometrial and ovarian tumors.

Materials and Methods: This was a retrospective study done in Department of Pathology, Tribhuwan University Teaching Hospital from September 2006 to August 2011. The datas were retrieved from computer database.

Results: There were totally of 10 cases of simultaneously detected endometrial and ovarian cancers. Out of 10 cases, 7 cases were synchronous primary endometrial and ovarian cancers while three were metastatic. Median age at presentation was 47.4 years. Six (85.8%) of these patients presenting with dual primary tumors were premenopausal. Grade 1 histology was seen in 57% of endometrial and 42% of ovarian tumors. Atypical endometrial hyperplasia was found in 42.8% of cases while none of the cases showed endometriosis.

Conclusion: Though limited by relatively small number of cases, younger and premenopausal women were predisposed to developing synchronous primary tumors of the endometrium and ovary.

INTRODUCTION

Primary synchronous cancers of the female genital tract are a relatively uncommon comprising 1-6% of all genital neoplasms. Amongst these, simultaneously detected endometrial and ovarian malignancies constitute the commonest occurrence.[1]

Synchronous tumors can be classified into three groups[2]

1. Endometrial cancer with metastasis to the adnexa.
2. Ovarian cancer with metastasis to the endometrium.
3. Synchronous primary tumors.

Correspondence:
Dr. Shovana Karki, MD
Department of pathology, Tribhuwan University Teaching Hospital, Kathmandu, Nepal.
Email: shovana_karki@hotmail.com

A set of pathological criteria was devised by Ulbright and Roth for distinguishing metastatic tumors from synchronous primary tumors.[3] Scully et al described a more extensive list of clinicopathological features to differentiate endometrial tumors metastatic to ovary (Table 1), ovarian tumor metastatic to endometrium (Table 2), and independent primary cancers (Table 3).[4] Various studies suggest that women with synchronous primary cancers have a better overall prognosis than if their disease was classified as single organ tumor with metastasis.[5-7] Currently, differentiating a single primary with metastasis from dual primary cancer involves clinicopathological correlation. But in some cases establishing the relation between co-existing ovarian and endometrial cancers with certainty may still be a diagnostic challenge.[8] The purpose of this study was to characterize patients with synchronous primary endometrial and ovarian tumors.

Table 1: Endometrioid tumors of the ovary and endometrium[4]

Endometrial primary, ovarian secondary	
1.	Histologic similarity of the tumors
2.	Large endometrial tumor – small ovarian tumor
3.	Atypical endometrial hyperplasia additionally present
4.	Deep myometrial invasion Direct extension into the adnexa Vascular space invasion in myometrium.
5.	Spread elsewhere in typical pattern of endometrial carcinoma
6.	Ovarian tumor bilateral and/or multinodular
7.	Hilar location, vascular space invasion, surface implants or combination in ovary
8.	Ovarian endometriosis absent
9.	Aneuploidy with smiliar DNA indices or diploidy of both tumors[a]
10.	Smiliar molecular genetic or karyotypic abnormalities in both tumors

Table 2: Endometrioid tumors of the ovary and endometrium[4]

Ovarian primary, endometrial secondary	
1.	Histologic similarity of the tumor
2.	Large ovarian tumor – small endometrial tumor
3.	Ovarian endometriosis present
4.	Location in ovarian parenchyma
5.	Direct extension from ovary predominantly into outer wall of uterus
6.	Spread elsewhere in typical pattern of ovarian carcinoma
7.	Ovarian tumor unilateral (80-90% of cases) and forming single mass
8.	No atypical hyperplasia in endometrium
9.	Aneuploidy with smiliar DNA indices or diploidy of both tumors[a]
10.	Smiliar molecular genetic or karyotypic abnormalities in both tumors

Table 3: Endometrioid tumors of the ovary and endometrium[4]

Independent primary tumors	
1.	Histologic dissimilarity of the tumors
2.	No or only superficial myometrial invasion of endometrial tumor
3.	No vascular space invasion of endometrial tumor
4.	Atypical endometrial hyperplasia additionally present
5.	Absence of other evidence of spread of endometrial tumor
6.	Ovarian tumor unilateral (80-90% of cases)
7.	Ovarian tumor located in parenchyma
8.	No vascular space invasion, surface implants, or predominant hilar location in ovary
9.	Absence of other evidence of spread of ovarian tumor
10.	Ovarian endometriosis present
11.	Different ploidy of DNA indices, if aneuploid, of the tumorsa
12.	Dissimilar molecular genetic or karyotypic abnormalities in the tumors

Table 4: Characteristic of endometrial cancer

	No. of cases (%)
Cell type	
Endometrioid	7 (100%)
Non endometrioid	0
Histological grade	
1	4 (57.2%)
2	2 (28.6%)
3	1 (14.2%)
Vascular invasion	
Yes	1 (14.2%)
No	6 (85.8%)
Depth of myometrial invasion	
None	0
<50	5 (71.4%)
>50	2 (28.6%)
Adjacent endometrial hyperplasia	
Yes	3 (42.8%)
No	4 (57.2%)

Table 5: Characteristics of ovarian tumor

	No. of cases (%)
Cell type	
Endometrioid	7 (100%)
Non endometrioid	0
Bilateral involvement	
Yes	0
No	7 (100%)
Surface involvement	
Yes	0
No	7 (100%)
Vascular invasion	
Yes	2 (28.6%)
No	5 (71.4%)
Tubal lumen involvement	
Yes	0
No	7 (100%)
Endometriosis	
Yes	0
No	7 (100%)

MATERIALS AND METHODS

This was a retrospective study in which 10 cases of simultaneously detected endometrial and ovarian cancers from September 2006 to August 2011, in the Department of Pathology, Tribhuvan University Teaching Hospital were included for study.

Diagnosis of endometrial and ovarian tumors was made on the basis of WHO criteria.[4] Pathologic characteristics such as histology of primaries, depth of myometrial invasion, grades, lymphovascular invasion, presence of endometrial hyperplasia or endometriosis for endometrial and ovarian tumors, were collected from computer database. Datas were analyzed by using software SPSS 10.0 version.

RESULTS

There were 10 (0.03%) cases of simultaneously detected endometrial and ovarian cancers. Out of 10 cases, 7 cases were synchronous primary endometrial and ovarian cancers while 3 were metastatatic cancers. Age ranged from 37-51 years with a median age of 47.4 years for synchronous primary tumors. Six of these patients presenting with dual primary tumors were premenopausal. In the metastatic group, the median age at presentation was 59.4 years and all 3 patients were postmenopausal. The macroscopic and histopathologic features of endometrial and ovarian tumors are summarized in Table 4 and Table 5. Comparisons of coexisting tumors are shown in Table 6.

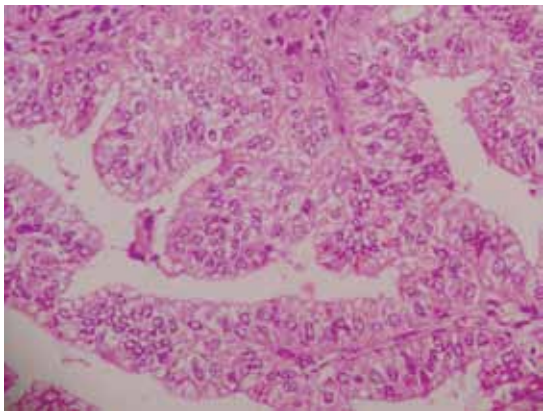

Figure 1: Endometrioid carcinoma of endometrium, grade 1, showing secretory changes (HE stain, X200).

DISCUSSION

The occurrence of coexisting primary malignancies of the female genital tract and their distinction from metastatic disease is a challenging subject in gynecologic oncology as it has associated prognostic and therapeutic significance. In the present study, the age range of patients with synchronous primary cancers was 37-51 years with a median age of 47.4 years, whereas in the metastatic group it was 59.4 years. Other studies have demonstrated median age ranging from 41-54 years.[2,5,9] It is worth mentioning that 6 (85.8%) of the patients with synchronous primaries were premenopausal while all patients with metastasis were post menopausal. In a similar study, it was found that 16/30 cases (53%) with synchronous primary tumors were premenopausal.[10]

The presence of precancerous histological features generates a strong evidence of in situ genesis rather than metastasis in endometrium and ovaries. Presence of atypical endometrial hyperplasia or endometriosis suggests de novo development of cancers in endometrium and ovary respectively.[1,11] In this study atypical endometrial hyperplasia was found in 3 cases while none of the cases showed endometriosis. In a similar study 14/30 cases had histological evidence of endometrial hyperplasia and 8/30 had endometriosis.[10]

All 7 cases of synchronous primaries were of endometrioid cell type (fig.1) and all of the tumors were concordant in both sites. In another study 90% of the dual primaries were endometrioid cell type and the cell type was concordant in both sites in 93% of the cases.[1] This is about the expected frequency of adenocarcinoma arising in the endometrium while serous carcinoma is the commonest cell type of carcinoma arising in the ovary in isolation.[1]

Most of the tumors were histological Grade 1 in both the endometrium (57%) and ovary (42%) This distribution of histological grade is similar to the study of Zaino et al[1] and Eifel et al.[5] It has been found in other studies that well differentiated tumors were associated with lower probability of recurrence but the cell type did not contribute significantly to the prediction of recurrence.[1]

According to the criteria of Ulbright and Roth[3], features favoring metastasis like multinodular configuration of ovary, ovarian size <5 cm, bilateral ovarian involvement, vascular invasion and tubal involvement were rare. Furthermore, endometrial hyperplasia and superficial myometrial invasion which are commonly seen in carcinoma arising in the endometrium were frequently observed in the uteri whereas vascular invasion was rare. All these observations suggest that these cases represent simultaneous development of carcinomas in both the endometrium and ovary. Similar

Table 6: Coexisting endometrial and ovarian cancers

Case #	Endometrium			Ovary		
	Histologic type	Grade	TNM/FIGO	Histology type	Grade	TNM/FIGO
1	E	1	T1a/IA	E	1	T1a/IA
2	E	1	T1a/IA	E	1	T1a/IA
3	E	1	T1a/IA	E	1	T1a/IA
4	E	1	T1a/IA	E	2	T1a/IA
5	E	2	T1b1/IB	E	2	T1a/IA
6	E	2	T1a/IA	E	3	T1a/IA
7	E	3	T1a/IB	E	3	T1a/IA

E: endometroid type

results were obtained in a study carried out by Chen et al.[12]

Synchronous primary cancers of the endometrium and ovary in this series presented at an earlier stage. In several other studies also presentation of these dual primary cancers at an earlier stage was seen.[10,12] Typically it is noted that isolated ovarian cancers are usually diagnosed at advanced stages due to the non specific symptoms of the disease.[13]

Several molecular studies have supported the hypothesis of independent origin by demonstrating different patterns of X chromosome inactivation and dissimilar mutations in PTEN, p53 or K-ras.[14-16] Only 53% concordance rate between genetic and histopathologic diagnosis for synchronous primary tumors was seen in a study based on loss of heterozygosity pattern.[17]

Although a variety of clinical and pathologic characteristics have been proposed for the determination of the origin of such dual primaries, it is not certain whether all these features are always able to distinguish synchronous primaries from metastasis from one site to another. In such cases, it seems that genetic studies and molecular analysis will further help in characterizing and favoring the diagnosis of synchronous primary tumor over metastasis.

CONCLUSION

Overall survival and progression free survival of synchronous primary cancers in patients with endometrial cancer is better than those with ovarian metastasis. Metastasis represents an advance stage cancer with requirement of more aggressive therapy. Thus the diagnosis given will influence the patients' treatment and outcome. Hence, it is recommended to categorize patients with synchronous primary tumors of the endometrium and ovary.

REFERENCES

1. Zaino R, Whitney C, Brady M, Degeest K, Burger R, Buller R. Simultaneously detected endometrial and ovarian carcinomas – a prospective clinicopathologic study of 74 cases ; a Gynecologic Oncology group Study. Gynecol Oncol 2001;83:355-62.
2. Soliman PT, Solmovitz BM, Broaddus RR et al. Sychronous primary cancers of endometrium and ovary: a single institution review of 84 cases. Gynecol Oncol 2004;94:456-62.
3. Ulbright T, Roth L. Metastatic and independent cancers of the endometrium and ovary; A clinicopathologic study of 34 cases. Hum Pathol 1985;16:28-34.
4. Scully R E, Young R H, Clement PB, editor. Atlas of Tumor Pathology, Tumors of the ovary, maldeveloped gonads, fallopian tube, and broad ligament. 3rd Series, Fascicle 23. Armed Forces Institute of Pathology:Washington, DC; 1998. 126pp.
5. Eifel P, Hendrickson M, Ross J, Ballon S, Martinez A, Kempson R. Simultaneous presentation of carcinoma involving the ovary and uterine corpus. Cancer 1982;50:163-70.
6. Zaino R, Unger E, Whitney C. Synchronous carcinomas of the uterine corpus and ovary. Gynecol Oncol 1984;19:329-35.
7. Montoya F, Martin M, Schneider J, Matia JC, Rodriguez-Escudero FJ. Simultaneous appearance of ovarian and endometrial carcinoma: a therapeutic challenge. Eur J Gyanecol Oncol 1989;10:135-9.
8. Ramus SJ, Elmasry K, Luo Z et al. Predicting clinical outcome in patients diagnosed with synchronous ovarian and endometrial cancer. Clin Cancer Res 2008;4:5840-8.
9. Ree YS, Cho SH, Kim SR, Kim KT, Park MH. Synchronous primary endometrial and ovarian cancer with three histologic patterns: a case report. Int J Gynecol Cancer 2003;13:678-82.
10. Rodolakis A, Thomakos N, Akrivos N et al. Clinicopathologic insight of simultaneously detected primary endometrial and ovarian carcinomas. Arch Gynecol Obstet 2011 Aug 14 [Epub ahead of print].
11. Falkenberry SS, Steinhoff MM, Gordinier M, Rappoport S, Gajeewski W, Granai Co. Synchronous endometrioid tumors of the ovary and endometrium. J Reprod Med 1996;41:713-18.
12. Chen L, Zhao Q, Lv X. Characteristics and prognosis of coexisting adnexa malignancy with endometrial cancer: a single institution review of 51 cases. Arch gynecol Obstet 2011;283:1133-7.
13. Barakat RR, Grigsby PW, Sabbatini P, Zain RJ. Corpus: epithelial tumors. In: Hoskins W, Perez C, Young R (eds). Principles and practice of gynecologic oncology. Lippincott, Philadelphia; 2000. pp 919-60.
14. Fujita M, Enomoto T, Wada H, Inoue M, Okudaira Y, Shroyer KR. Application of clonal analysis: differential diagnosis for synchronous primary ovarian and endometrial cancers and metastatic cancer. Am J Clin Pathol 1996;105:350-9.
15. Lin Wm, Forgacs E, Warshal Dp et al. Loss of heterozygosity and mutational analysis of the Pten/MMAC 1 gene in synchronous endometrial and ovarian carcinomas. Clin Cancer Res 1998; 4:2577-83.
16. Caduff RF, Svoboda-Newmas SM, Bartos Re, Ferguson AW, Frank TS. Comparative analysis of histologic homologues of endometrial and ovarian carcinoma. Am J Surg Pathol 1998; 22:319-26.
17. Brinkmann D, Rayan A, Mc Cluggage WG et al. A molecular genetic and statistical approach for diagnosis of dual site cancers. J Natl Cancr Inst 2004; 96: 1441-6.