

Synchronous endometrioid carcinoma of bilateral ovaries and uterus: A case report

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Received: May 14, 2018; Accepted: May 31, 2018

ABSTRACT

Synchronous primary cancer of female genital tract is relatively uncommon; about 0.5–1.7% of women with gynecological malignancies have synchronous primary cancers of the female genital tract. Synchronous primary endometrial and ovarian cancers are the most common combination, and among them, synchronous endometrioid carcinoma is common and has good prognosis. Here, we presented the case of a 45-year-old woman with heaviness in the abdomen. On ultrasonography, there was bilateral massive enlargement of ovaries with polypoidal growth in the uterus. Histopathology revealed synchronous endometrioid carcinoma of both ovaries and uterus.

KEY WORDS: Endometrioid Carcinoma; Bilateral Ovaries; Synchronous

INTRODUCTION

Synchronous primary cancers are relatively uncommon in general population. About 0.5–1.7% of women with gynecological malignancies have synchronous primary cancers of the female genital tract. Synchronous primary endometrial and ovarian cancers are the most common combination.^[1]

Patients with synchronous endometrioid tumors of the endometrium and ovary are generally younger, tend to be of low grade, and the prognosis of endometrioid type carcinoma is better than other histological types of carcinoma.


It is challenging diagnostically and therapeutically when there is similar histology. There are many gross and microscopic

features which help in distinction between synchronous primaries and metastasis. Immunohistochemistry plays an important role to differentiate single primary with metastasis and dual primaries, but due to poor patient and limited resource, immunohistochemistry could not be done.

CASE REPORT

The patient was referred to our hospital with complaint of lower abdominal pain and heaviness of 2–3 weeks duration. On clinical examination, there was palpable mass in lower abdomen extending up to umbilicus. On per vaginal examination, cervix was normal, and on per speculum examination, tumor-like tissue was in the vaginal cavity extending from the uterus. Computed tomography scan revealed solid cystic bilateral ovarian mass. On the right side, it was 13.8 cm × 12.7 cm × 16.5 cm, and on the left side, it was 15.4 cm × 11.8 cm × 13.1 cm. Both masses were adherent to each other. The uterus was bulky and contained thick endometrium. Cervix was normal.

Her laboratory investigations were all within the normal limits apart from high levels of cancer cell surface antigen 125 (CA125) of 576 IU/l.

Access this article online	
Website: http://www.ijmsph.com	Quick Response code 
DOI: 10.5455/ijmsph.2018.0516631052018	

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On gross examination, both ovaries were solid-cystic components with large areas of necrosis and abundant mucoid sticky material came out. Uterine cavity revealed polypoidal tumor.

Histopathological examination showed well-differentiated bilateral endometrioid ovarian carcinomas and moderately differentiated adenocarcinoma of uterus infiltrating up to two-thirds of the depth of uterine wall [Figures 1-4].

DISCUSSION

Endometrial carcinoma is the third most common genital malignancy in women after cervix and ovary. Among all types, endometrioid adenocarcinoma is the most common histological subtype comprising 75–80%, serous papillary carcinoma 5–10%, and clear cell carcinoma 3–5%. Serous papillary carcinoma and clear cell carcinomas are aggressive types.^[2]

The average age at diagnosis is 60 years. Women diagnosed with endometrial cancer younger than 40 years make up only

5%. They invariably have specific risk factors such as morbid obesity, chronic anovulation, and hereditary syndromes.

The differentiation of endometrial cancers is one of the most important prognostic factors. Grade 1, 2, and 3 endometrial adenocarcinomas make up 45, 35, and 20%, respectively. The 5-year survival rate of Stage I cancer is 94%, 88%, and 79% for Grade 1, 2, and 3 tumors, respectively. High tumor grade, advanced surgical stage, and lymphovascular space invasion have been implicated as poor prognostic factors for dissemination of disease.^[2]

Ovarian endometrioid carcinomas account for only 10% of ovarian carcinomas. The majority of ovarian carcinomas (70-80%) are high-grade serous carcinomas which are aggressive in nature and have poor outcomes. The majority of ovarian endometrioid carcinomas, like endometrial endometrioid carcinomas, are also low-grade with good prognosis. Endometrioid carcinomas of the ovary and endometrium are both described to contain *PTEN*, *PIK3CA*, *ARID1A*, *PPP2R1A*, and *CTNNB1* (β -catenin) mutations. However, the frequency of mutations differs in these tumor

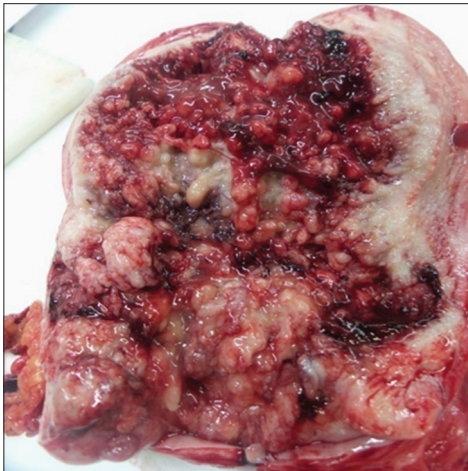


Figure 1: Gross image of uterine tumor

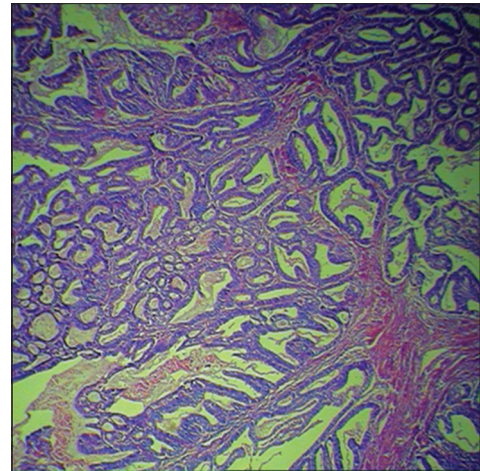


Figure 3: H and E staining of uterine tumor



Figure 2: Gross image of ovarian tumor

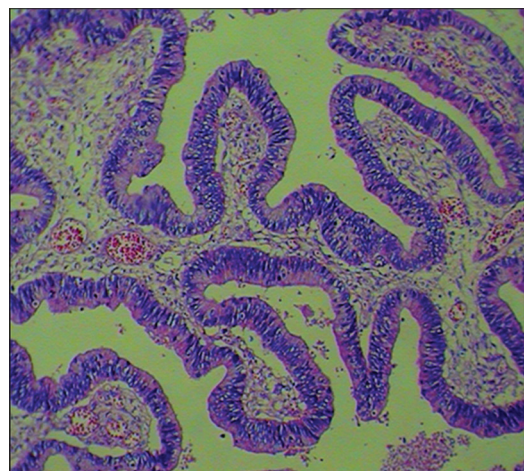


Figure 4: H and E staining of ovarian tumor

types.

According to the literature, most patients with synchronous cancers present symptoms characteristic of endometrial cancer.^[3] The most frequently reported symptoms are abnormal vaginal bleeding (42–70%), pain in lower abdomen (17–44%), palpable tumor in pelvis (28–40%), and increased serum concentration of CA125 (65%).^[4–7]

It is also possible that synchronous presence of these cancers is an indicator of an etiologically distinct condition. Perhaps, patients have a more fragile genome and prior genetic damage may predispose to synchronous cancers. Thus, embryologic, hormonal, or other phenomena may be associated with the development of malignancies arising simultaneously in genital tissues.^[1]

Several histological features help distinguish primary from metastatic tumors in the endometrium and ovaries. The presence of a precancerous process is a strong evidence of *in situ* genesis. In the endometrium, these processes include endometrial hyperplasia, especially if atypical, or the recent and more narrowly defined lesion, endometrial intraepithelial neoplasia. Similarly, the presence of potentially precancerous processes in the ovary such as endometriosis or a preexisting benign or borderline tumor of similar histological type suggests *de novo* development of the cancer also in the ovary. Different histological types (but not grade) of synchronous endometrial and ovarian tumors are also good evidence of independent primaries. On the other hand, similar histology cannot be taken as evidence of metastasis from one organ to the other. About 15–25% of ovarian tumors with endometrioid histology are associated with a histologically similar lesion in the endometrium. These lesions are usually regarded as well-differentiated independent neoplasms because of their high survival rates.^[8] In our case, patient directly presented with such mass without any prior history of precursor lesion.

Tumor in the lumen of the fallopian tubes suggests metastasis. This is most often associated with serous tumors arising in the endometrium that implants on the ovary by retrograde transmission. Synchronous tumors that are regarded as metastases are usually of high histological grade, for example, adenosquamous carcinomas, mixed Mullerian tumors, and non-endometrioid carcinomas (serous and clear cell). In our case, both ovaries were without any surface nodules.^[8]

Microscopic features that raise the possibility that an ovarian tumor might be metastatic include a bilateral, multinodular growth pattern, implants on the surface of the ovary, and numerous emboli of metastatic carcinoma in lymphatic spaces, especially in the hilum and mesovarium, and an unusual microscopic pattern for a primary ovarian tumor, such as goblet cells in an inappropriate histologic setting, a signet ring cell appearance, or an Indian file pattern of invasion,^[9] but in this case, all features were absent except

bilateral involvement.

Synchronous tumors can be classified into three groups:

1. Endometrial cancer with metastasis to the adnexa.
2. Ovarian cancer with metastasis to the endometrium.
3. Synchronous primary tumors.^[10]

Patients with synchronous primary endometrial and ovarian cancers have distinct clinical characteristics including young age, obesity, premenopausal status, and nulliparity. Usually, they are 10–20 years younger than patients with single endometrial or ovarian cancer. The median age at diagnosis is 50 years.^[11]

The pathogenesis of synchronous primary endometrial and ovarian cancers remains unclear. The theory of the secondary Müllerian system has been proposed to explain the development of synchronous primary cancers in the female genital tract. According to this theory, the epithelia of the upper female genital tract have common embryologic origin and respond as a morphologic unit to a carcinogenic stimulus (hormone, radiation, and other). Perhaps, shared hormone receptors (estrogen receptors) are responsible for the development of synchronous primary cancers in the female genital tract.^[11]

In large studies, the endometrioid type is low grade, and the early stage of synchronous endometrioid ovarian carcinomas is associated with a better prognosis and an overall survival of 80–90% in contrast to the poor prognosis noted in metastatic disease.^[12,13]

Surgery is mandatory in operable stages of endometrial and ovarian cancers. Optimal extent of the operation in endometrial cancer covers panhysterectomy, peritoneal cytology, and pelvic lymphadenectomy. In the case of abdominal metastases, para-aortic lymphadenectomy, omentectomy, and metastasectomy are indicated. This extended surgery is always indicated in patients with operable ovarian cancer. Nowadays, total laparoscopic hysterectomy with lymphadenectomy is often carried out instead of laparotomy in the case of endometrial cancer. The benefits associated with this procedure are shorter hospital stay and fewer complications, but its main drawbacks are longer duration of surgery and more expensive equipment. The choice of adjuvant therapy in most cases of synchronous cancers depends on the stage and grade of ovarian cancer. The use of radiotherapy in patients with the synchronous cancers, who are treated with adjuvant chemotherapy, is controversial.^[14]

CONCLUSION

It is very important to identify synchronous primaries and metastatic tumors correctly as staging, prognosis, and further management depend on it. In fact, standard criteria for differentiating between primary and metastatic tumors may be

misleading in this situation, and additional testing is required. IHC and recently molecular diagnosis will provide the final confirmation. However, in set up with limited resources, gross with histopathology in background of other clinical data helps to reach final diagnosis in most of the cases.

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How to cite this article: Shah NC, Polra JH. Synchronous endometrioid carcinoma of bilateral ovaries and uterus: A case report. *Int J Med Sci Public Health* 2018;7(9):770-773.

Source of Support: Nil, **Conflict of Interest:** None declared