International Journal of Clinical Obstetrics and Gynaecology

ISSN (P): 2522-6614
ISSN (E): 2522-6622

www.gynaecologyjournal.com
2024; 8(4): 189-192
Received: 13-06-2024
Accepted: 18-07-2024

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Synchronous endometrial and ovarian cancer: A case report

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DOI: https://doi.org/10.33545/gynae.2024.v8.i4c.1496

Abstract
Synchronous endometrial and ovarian cancer (SEOC) is a rare genital tract tumour. It should be differentiated from primary endometrial or ovarian tumours with metastasis since the two entities have different therapeutic and prognostic implications. In this review we present a case of woman who was diagnosed with SEOC, and discuss the clinical characteristic of SEOC, diagnostic and molecular profiling issues Next generation sequencing of 10 gene panel was performed on cancerous tissue and uterine lavage samples.

Keywords: Carcinoma, endometrial, ovarian, primary, synchronous

Introduction
Synchronous tumors of the female genital tract are rare comprising only about 1% of all genital malignancies [1]. The most common synchronous tumor is synchronous endometrial and ovarian cancer which accounts for 50%-70% of all [1]. However, most cases are metastatic arising from one organ and simultaneous primary cancer involving both organs is uncommon [2]. The incidence of synchronous primary endometrial and ovarian carcinoma (SPEOC) is limited and it can easily be confused with endometrial cancer with ovarian metastasis [3]. Thus, it is important to diagnose such separate independent primary tumours and mandates careful consideration of the number of lesions, and histological and immunohistochemical features as the two entities have different therapeutic and prognostic implications.
We report a case of a 60-year-old woman with synchronous primary endometrial and left ovarian carcinoma.

Case report
A 60 yr old nullipara female presented with post-menopausal bleeding since 4 days. She used 1 pad per day which was also not completely soaked. There was no history of any abdominal pain or vaginal discharge. There was no other illness or history of any malignancy in the family.
On examination, she had a BMI of 25.5 kg/m^2 and her vitals were normal. Per abdominal examination was unremarkable. Per speculum examination revealed a healthy cervix with a bloodstain. On per vaginal examination, there was a right adnexal mass around 5 × 5 cm, firm to solid cystic, smooth, mobile, and non-tender with the groove felt between the mass and uterus. Routine investigations and tumour markers were sent with suspicion of an ovarian mass. (Table 1).

Table 1: Comparison of patient's tumour marker levels with corresponding reference levels.

Tumour marker	Patient's level	Reference level
LDH	428 U/L	140-280 U/L
Beta HCG	1.8 mIU/ml	<5 mIU/ml
CA 125	52 U/ml	<35 U/ml
CEA	4.5 ng/ml	<3 ng/ml
AFP	3.28 ng/ml	<7.51 ng/ml

Abdominal ultrasound was done. Pelvic collection was seen with probe tenderness S/O pelvic lymphadenopathy. Rt ovary was not separately visible.

Hysteroscopy was done. Cervix and vagina were normal looking. Endometrium was irregular and hypertrophic all over. Endometrial biopsy was taken which showed atypical endometrial hyperplasia.

MRI revealed ill-defined heterogeneous mass around 4.4x 3.4x 3.2 cm in endometrial canal S/O endometrial carcinoma and lobulated solid lesion in right adnexa around 5.5x 4.7x 5.1 cm S/O right ovarian carcinoma. CT scan also revealed atrophied uterus with adherent bowel loops in right adnexa.

After the positive frozen section pathological examination in the ovaries, the patient underwent total abdominal hysterectomy with bilateral salpingo-oophorectomy with bilateral pelvic and para-aortic lymphadenectomy, omentectomy and peritoneal biopsies. (Figure 1) Intraoperatively, there was an irregular mass of around 6 × 5 x 4 cm arising from the right ovary. A cross-section of the ovary revealed fatty material and mucoid material inside. The uterus was 10 cm with the body and cervix 7 and 3 cm respectively with a rough towel appearance. Myometrial thickness was 1 cm with endometrial hyperplasia noted. The endocervical canal was empty. Her post-operative period was unremarkable and was discharged on the 5th postoperative day.

Histopathology of the excised specimens revealed endometrial adenocarcinoma and right ovarian adenocarcinoma with histological grade 2. The tumour was limited to the inner half of the myometrium and 5 mm within the capsule of the ovary. Lymphovascular invasion was not seen. (Figures 1 and 2) Owing to the financial constraint and unavailability of immunohistochemical analysis, the immunotyping of the tumour was not performed. Peritoneal cytological washing and biopsies, as well as lymph nodes, were negative for malignant cells. The final diagnosis of synchronous FIGO Ia endometrial adenocarcinoma and FIGO Ia ovarian adenocarcinoma was made. The patient is disease-free at 6 months of follow-up with no evidence of recurrence.

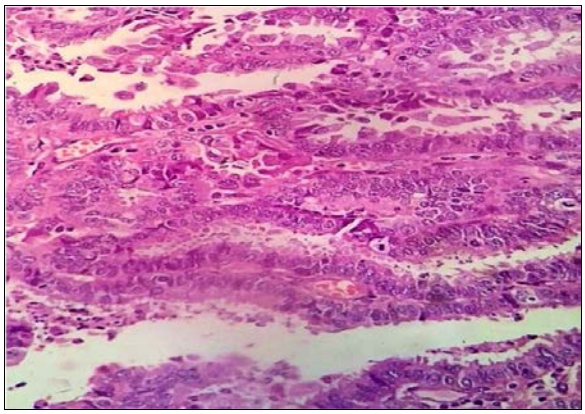

Fig 1: Section from right ovary shows tumour cells arranged in papillae, tubules, and micropapillae showing moderate atypia. Tumour cells have a moderate amount of eosinophilic to granular cytoplasm, vesicular nuclei, and inconspicuous nucleoli without capsular invasion

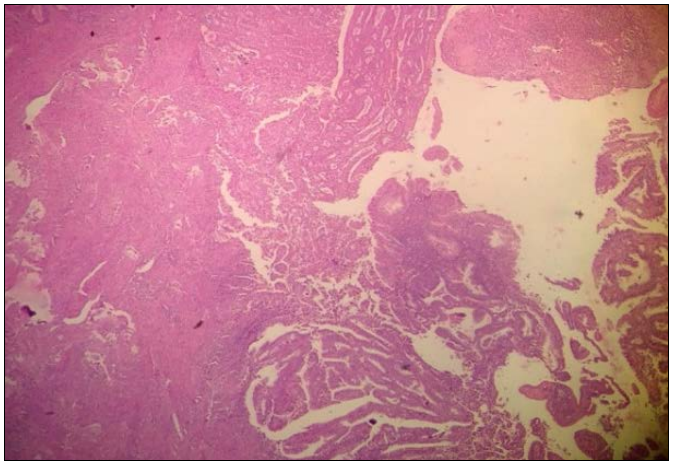

Fig 2: Section from endometrium shows tumour cells lined by pseudostratified columnar epithelium showing mild nuclear polymorphism. Invasion into less than half of the myometrium is seen without lymphovascular and perineural invasion

Discussion

SPEOC is found in approximately 5% of all females with endometrial cancer and 10% of all females with ovarian cancer. Due to its rarity, it is often misdiagnosed as FIGO stage III of endometrial cancer or FIGO stage II of ovarian cancer [3].

SEOC is usually observed among the younger age women under 55 years and 40% of them are nulliparous as in this case. In most cases it can be diagnosed at an early stage and is associated with low-grade disease. The endometrioid subtype of the primary tumors is the most common histological finding with the rate of 50%-70% of cases.

Abnormal uterine bleeding is the most common presentation of synchronous endometrial and ovarian cancer, though some patients may present with pelvic pain or a palpable pelvic mass [4].

The development of the surface epithelium of the ovary from the embryological Mullerian duct and sharing of estrogen receptors in predisposed tissues are the likely reasons for their synchronous growth [5]. In our case, histology revealed no evidence of metastasis as the tumor from the section of endometrium was limited to the inner half of the myometrium and within the capsule of the ovary without lymphovascular invasion.

Advancement of immunohistochemistry and molecular testing is needed to determine cancer origin accurately. According to literature it is suggested that immunohistochemistry testing of vimentin can be carried out. Desouki *et al.* [6] suggested that a negative stain has a sensitivity and specificity to predict primary OC at 97% and 82%, while positive vimentin staining had an 82% sensitivity and 97% specificity in predicting EC. Another study used different antibodies (ER, PR, HER2, p53, and Ki-67) and they found that ER, PR, BCL2 showed different immunostaining patterns between EC and OC and suggested that they can be used as a surrogate marker in the distinction of these tumors [7].

Using FIGO guidelines, a patient with dual primaries limited to the ovary and the uterus represents two Stage I cancers. Systematic surgical staging is the mainstay of the management for such patients and often includes total abdominal hysterectomy with bilateral salpingo-oophorectomy, total omentectomy, pelvic and para-aortic lymphadenectomy, and complete resection of all diseases [5]. Our patient too underwent the aforementioned staging surgery.

Based on histological findings alone, synchronous uterine and ovarian endometrioid carcinoma is considered when all of the following criteria are met: Both tumors are low grade (FIGO 1 or 2); less than 50% of myometrial invasion is present; ovarian tumor is unilateral, limited to parenchyma and no other site is involved in a malignant process; extensive lymphovascular invasion is absent at any location

These patients have a good prognosis and requirement of radio or chemotherapy depends on the substage. The treatment of respective cancer guides the adjuvant treatment. In endometrial cancer, chemotherapy is indicated when the risk of distant metastasis is high and in ovarian cancer, all but stage IA/B are to receive it [8]. Considering stage Ia of the ovarian tumor, adjuvant chemotherapy was not given to our patient.

The importance of distinguishing SEOC from either isolated endometrium or ovarian cancer with metastasis is crucial, as it determines adjuvant treatment strategy and prognosis. The prognosis of patients with synchronous EC and OC is better than the patients with single-organ cancer with ovarian or endometrial metastasis. Median 5-year progression free survival rate is reported to be less than 50% for FIGO stage IIIA EC with ovarian spread but it is 65% for SEOC. If SEOC is diagnosed in early stage the overall survival rate is excellent up to 90%, in contrast to the poor prognosis noted in metastatic disease [9, 10, 11]. Considering all, the prognosis of our patient is good and our patient is now disease-free at 6 months of surgery and is under regular follow-up.

Conclusion

The identification of SEOC or metastatic endometrium/ovarian disease has great clinical significance, as the disease management, prognosis and overall survival differ. Precise diagnosis of SEOC may require additional molecular or IHC testing in addition to routine histopathologic assessment. According to literature review testing of vimentin, molecular analyses of gene mutation of CTNNB1, PAX8, and β-catenin expression may be helpful to categorize SEOC particularly in cases where clinical and pathological parameters are inconclusive.

Consent

Written informed consent was obtained from the patient and her husband for publication of this case report and accompanying images.

Conflict of interest: The authors declare that they have no conflict of interest.

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How to Cite This Article
Yadav G. Synchronous endometrial and ovarian cancer: A case report. International Journal of Clinical Obstetrics and Gynaecology. 2024;8(4):189-192.