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## A rare presentation of synchronous primary endometrial and ovarian cancer

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### Abstract

Synchronous primary malignancies account for 0.7-1.8% of all gynecologic tumors. Synchronous endometrial and ovarian cancer (SEOC) is more frequent in younger, obese, premenopausal and nulliparous women. Organ-confined and low-grade synchronous endometrial and ovarian tumors (SEOs) clinically behave as independent primary tumors rather than a single advanced-stage carcinoma and have a better prognosis.

However differentiation between 1) primary ovarian tumor metastasizing to endometrium, 2) primary endometrial cancer metastasizing to ovary and 3) primary synchronous tumors of both endometrium and ovary is important as the management and prognosis is variable in all cases.

We here present a case of a 50 yr postmenopausal female presented with bleeding, diagnosed as endometrial adenocarcinoma on biopsy with no other organ involvement on imaging, underwent exploratory laparotomy with TAH with BSO with pelvic lymphadenectomy. On histopathology was diagnosed as endometrial adenocarcinoma with ovarian involvement, making a diagnosis to advanced stage endometrial cancer. On Immuno-histochemistry (IHC) was found to be synchronous primary ovarian and endometrial carcinoma stage 1, with no further treatment the patient was being followed up and is doing fairly well.

**Keywords:** Synchronous cancers, ovarian cancer, endometrial cancer, vimentin

### Introduction

Synchronous primary malignancies account for 0.7-1.8% of all gynecologic tumors. Synchronous ovarian and endometrial cancers (SEOC) comprise 40-53% of all synchronous gynecologic malignancies. Synchronous ovarian and endometrial cancers are found in 3.3-5% of all patients with endometrial cancer and in 2.7-10% of all patients with ovarian cancer [1].

According to the literature, most common symptom of patients with synchronous tumor is abnormal uterine bleeding which leads to earlier diagnosis in comparison to patients with primary ovarian tumor. Other symptoms with which the patient can present are lower abdominal pain, and signs of palpable tumor in pelvis and raised CA 125 levels.

The clinicopathological criteria given by Scully *et al.* [2] as well as Ulbright and Roth [3] to differentiate between synchronous primary tumors and single tumor with metastasis may not always be optimally applicable in every case and thus other molecular studies are required. At the molecular level, microsatellite instability (MSI), loss of heterozygosity (LOH) and PTEN mutational analysis and Vimentin expression by immunohistochemistry can be used as investigative tools in differentiating primary versus metastatic endometrioid carcinoma [4, 5].

The differential diagnosis between synchronous endometrial and ovarian cancers and endometrial cancer with ovarian metastasis has prognostic and therapeutic implications. Better prognostic outcome is seen in SEOC as against carcinoma endometrium with ovarian metastasis changing its staging.

### Case

A 50yr female postmenopausal since 2 yrs presented with history of per vaginal spotting on and off for 1 year. She was on ayurvedic treatment for these complaints for 1 year. Patient had history of irregular menses since 3-4 years prior to her menopause. Patient's mother had expired of lung cancer. She was para 1 living 1 full term vaginal delivery, with no sterilization done. She was obese with a weight of 102kg and BMI of 35.3 There were no significant findings on examination, uterus was bulky, free, fornices clear, cervix normal.

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Usg done prior to admission showed irregular thickened endometrium and a small anterior wall fibroid, rest of the scan was unremarkable. With a view to get a tissue diagnosis, curettage was done. Histopathological reporting was of an endometrial adenocarcinoma figo grade 1. Pap smear was normal.

In view of histopathology showing adenocarcinoma, patient was advised to undergo an MRI pelvis with abdominal screening for staging of disease. This helped in planning the further management. MRI showed a bulky uterus with large heterogeneously enhancing lesion in fundus and body of uterus 3.6\*5.1. \*4.5cm with > 50% myometrial invasion which was suggestive of a neoplastic lesion. Ovaries were reported normal with a few enlarged internal iliac lymph nodes.

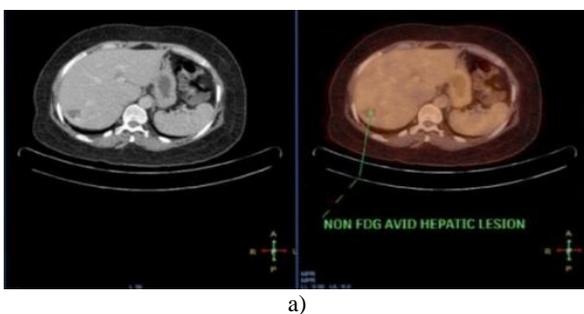
PET CT was done by the patient on seeking a second opinion from another doctor, which showed metabolically active lesion involving endometrium. After reviewing the case we decided to perform exploratory laparotomy with staging and intraoperative analysis. Exploratory laparotomy with pan hysterectomy with pelvic lymphadenectomy was done.

The histopathology revealed Endometrioid adenocarcinoma FIGO grade 1 involving endometrium (<50% thickness of myometrium) and right ovary showed well differentiated endometrial adenocarcinoma. With a possibility of synchronous tumor in mind further IHC was done (vimentin stain, with a rationale that endometrium is vimentin positive, while ovarian tissue is not). Tumor cells in ovary expressed ER(estrogen receptor) and PR(progesterone receptor) and focal vimentin, while endometrial tumor strongly expressed vimentin, thus suggesting synchronous primaries in endometrium and right ovary.

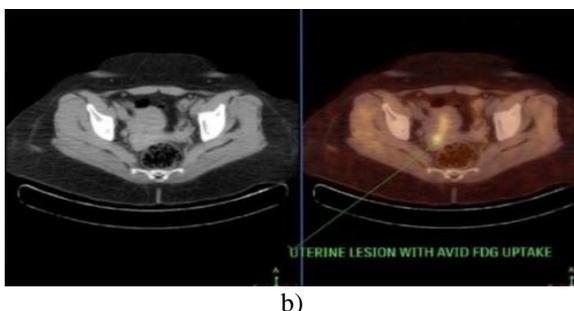
The 2.5\*2cm ovarian endometrioid adenocarcinoma was well differentiated, with intact capsule and only parenchymal microscopic tumor with no lymph nodes positive labeled as FIGO stage 1a.

Similarly the endometrioid endometrial adenocarcinoma was a well differentiated FIGO stage IA. The final diagnosis was synchronous primary endometrium and ovarian cancer stage 1.

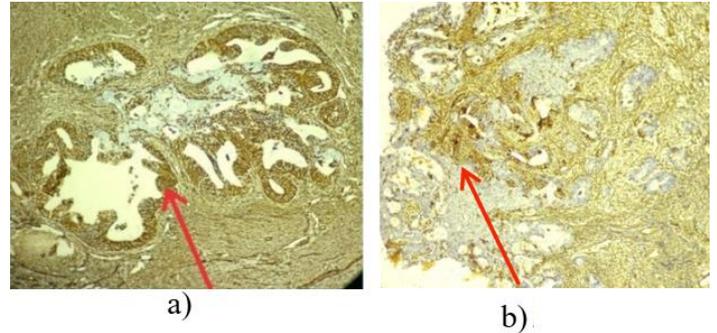
No postoperative chemotherapy or radiotherapy was given and the patient is doing fairly well with regular follow ups.



**Fig 1:** PET-CT shows avid FDG uptake in uterine cavity, active uterine lesion



b)



**Fig 2:** IHC slides: a) Endometrial tumor- Vimentin positive, b) Ovarian tumor- Vimentin negative

## Discussion

SEOC in patients appears with different clinical characteristics compared to patients with isolated EC (endometrial cancer)/ OC (ovarian cancer), and it is usually classified as a single-organ advanced disease.

An uncommon histological type of ovarian cancer is endometrioid type and it is thought to be developed under the same conditions as endometrial cancer [6]. Risk factors associated with synchronous ovarian and endometrial cancer are hyper estrogenic conditions such as: chronic anovulation, obesity, perimenopause, polycystic ovarian syndrome, unopposed estrogen replacement therapy and estrogen-producing ovarian tumors. This suggests that a hormonal “estrogenic effect” may account for the development of these simultaneous cancers [7].

Nearly 1 in 10 women under 50 years old that are diagnosed with EC will have a synchronous OC [6]. On the other hand, ovarian metastases have been reported to occur in about 5% of primary uterine cancers [8], therefore it is important to differentiate the two as it affects the subsequent treatment as well as the prognosis.

Scully *et al.* [2] defined the pathologic criteria for distinguishing between synchronous and metastatic disease updated by Ulbright and Roth [3]. The pathological criteria for synchronous primary cancers of the endometrium and ovary were as follows: 1) histological dissimilarity of tumors; 2) no (or superficial) myometrial invasion of endometrial tumor; 3) no lymphovascular space invasion in the uterine corpus or ovaries; 4) atypical endometrial hyperplasia additionally present; 5) absence of evidence of spread to other organs or tissues; 6) unilateral ovarian tumor (80-90% of cases); 7) ovarian tumors located mainly in parenchyma (no surface implants); 8) different DNA ploidy; 9) divergent molecular genetic or karyotyping abnormalities; and 10) endometriosis of ovary.

The differentiation of synchronous cancers from a single disseminated neoplasm is important, because it enables optimal adjuvant treatment, which further improves prognosis. According to different authors, a 5-year survival rate in patients with the synchronous cancers is 71-96% [1].

Patients presenting with abnormal uterine bleeding should undergo imaging test for assessment of ovaries; and patients presenting with an adnexal mass, should essentially undergo assessment of endometrium.

In our case the patient was diagnosed with endometrial adenocarcinoma and underwent exploratory laparotomy, while no imaging modality showed any ovarian involvement, and there were no other signs and symptoms apart from post menopausal bleeding.

Histopathology surprisingly showed ovarian endometrioid adenocarcinoma along with endometrial adenocarcinoma, thus

grading up the stage of cancer of endometrial cancer. Finally the diagnostic dilemma was solved by IHC which confirmed two separate primaries i.e. ovarian and endometrial adenocarcinoma stage 1, therefore adjuvant therapy was not required and patient was followed up regularly and is doing well.

The uniqueness of the case was that the patient presented with complains of post menopausal bleeding without other symptoms of an ovarian mass such as pain, pressure or mass effect. Also none of the imaging modality diagnosed an ovarian pathology. Vimentin staining clinched the diagnosis of SEOC as against advanced stage of endometrial cancer.

Primary ovarian and uterine endometrioid adenocarcinoma have different patterns of vimentin expression. The sensitivity and specificity of negative vimentin staining in predicting primary ovarian carcinoma were 97% and 82% respectively, and the positive vimentin staining in predicting primary uterine carcinoma were 82% and 97% respectively<sup>[4]</sup>.

The importance of differentiating SEOC from primary endometrium carcinoma with ovarian metastasis is that it changes management and prognosis.

### Conclusion

The diagnosis of synchronous endometrial and ovarian adneocarcinoma needs a wholistic consideration in terms of clinical & pathological features, imaging modalities, gross, microscopic and immunohistochemical factors as this has implications on staging, treatment and prognosis of the disease.

While involvement of ovaries is generally interpreted as metastatic disease or as a part of synchronous tumor, and the differential diagnosis often represents a clinical and histological challenge.

The synchronous cancers are usually diagnosed at an earlier stage and have lower grading, where surgical treatment alone may be enough thereby improving the prognosis, when compared to a single advanced cancer. Radiotherapy or chemotherapy may be required for advanced stages.

Also one should be vigilant to use other molecular diagnostic techniques to make a final diagnosis as further treatment and prognosis depends on it. Patients presenting only with postmenopausal bleeding without any other symptoms and signs of ovarian involvement may also present with synchronous tumors.

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