

Endometrioid Carcinoma of the Ovary and Uterus – Synchronous Primaries or Metastasis: A Case Report

ESWARI V., GEETHA PRAKASH, IRFAN A. ANSARI, BHANUMATHY V., GOMATHI PALVANNANATHAN

ABSTRACT

Synchronous endometrioid carcinoma of the uterine corpus and ovary is an uncommon but well known phenomenon. Such cases may represent either two primary tumours or a single primary and associated metastasis. There are significant clinical implications with either diagnosis. We present a case of a 48 year old unmarried women who came to our hospital with Right ovarian mass measuring 13cm. Total abdominal hysterectomy with bilateral salpingoophorectomy was done. Histological examination

showed well differentiated endometrioid ovarian cancer and well differentiated endometrioid endometrial cancer with squamous differentiation and metastasis of the endometrial cancer to the cervix. Patients with synchronous endometrioid tumours 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. Immunohistochemistry plays an important role to differentiate single primary with metastasis and dual primaries especially at places with limited resources.

Key Words: Synchronous primaries, ovarian cancer, Endometrial cancer

INTRODUCTION

The simultaneous development of multiple primary cancers in the upper female genital tract is a well known phenomenon. Of these the commonest is the endometrioid carcinoma of the ovary and the uterus. Diagnosis of this type of tumour either as a separate independent primary or as a metastatic tumour is difficult. A careful consideration of a number of gross, histological and immunohistochemical features may be helpful in the distinction between metastatic and synchronous primary tumours which have different therapeutic and prognostic implications [1, 2].

CASE REPORT

A 48 year old unmarried female was admitted in the Gynecology department of our hospital for abdominal distension of three days duration. Her menstrual periods were regular. Ultrasonography revealed a bulky uterus with a large complex right adnexal mass lesion arising from the ovary and extending across the midline.

Exploratory laparotomy with total abdominal hysterectomy with bilateral salpingoophorectomy was done.

GROSS

On gross examination uterus with cervix measured 9×7×4cm. C/S of the endometrium showed fleshy appearance with a friable growth extending up to the cervix [Table/Fig-1a].

The ovarian mass measured 13×6×4cm. E/S was smooth and there was no breach of the capsule. On C/S ovary was solid with few cystic areas and papillary projections. The cystic areas were filled with mucinous material [Table/Fig-1b].

The other ovary measured 2×2×1 cm. C/S showed corpus luteum. Also received omental fatty tissue measuring 11×6×1cm. Multiple sections were taken from the ovarian mass, cervix, endometrium and the omentum.



[Table/Fig 1a]: C/S of the endometrium showed fleshy appearance with a friable growth extending up to the cervix



[Table/Fig 1b]: Cystic areas were filled with mucinous material

MICROSCOPY

Histopathology of the ovarian mass revealed features of grade I endometrioid carcinoma with papillary change [Table/Fig-2a]. The tumour involved the entire thickness of the ovary. Vascular, lymphatic or capsular invasion was not seen and coexistent endometriosis was not seen. Sections from the endometrium also revealed features of grade I endometrioid carcinoma with focal squamous differentiation and infiltration into myometrium [Table/Fig-2b&c]. Sections from the cervix showed an endocervical endometrioid carcinoma [Table/Fig-2d]. Serial sections from the tubes showed normal histology. Sections from omental pad of fat were free from any tumour deposit.

IMMUNOHISTOCHEMISTRY(IHC)

To rule out metastasis from primary we proceeded with IHC using vimentin, epithelial membrane antigen (EMA) and cytokeratin (CK) as basic markers. The endometrial and the cervical tumours were positive for vimentin and EMA, while cytokeratin was positive in squamous differentiation in endometrium and it was negative in the cervix [Table/Fig-3]. The ovarian mass was positive for EMA and CK and negative for Vimentin [Table/Fig-4].

DISCUSSION

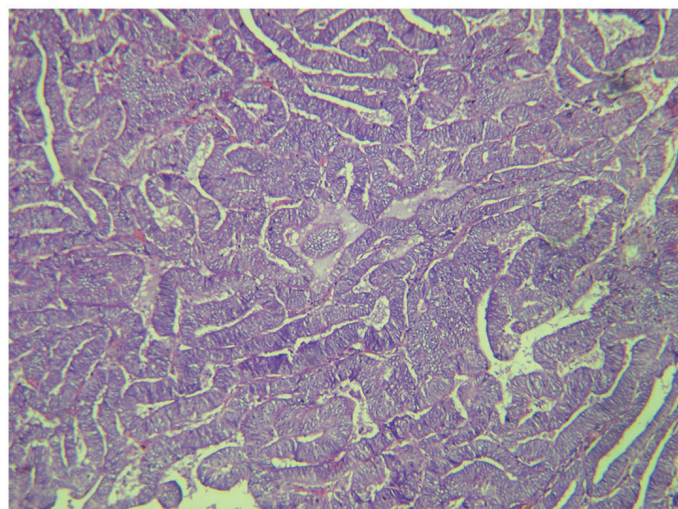
The presence of two genital tumours at the same time is relatively uncommon. They make 0.63% of all genital malignancies [3]. Carcinoma of the ovary and the endometrium can occur simul-

atenously in about 10% of women with ovarian carcinoma [4]. This may be attributed to the development of the surface epithelium of the ovary which has the same embryologic derivation from the mullerian duct [1].

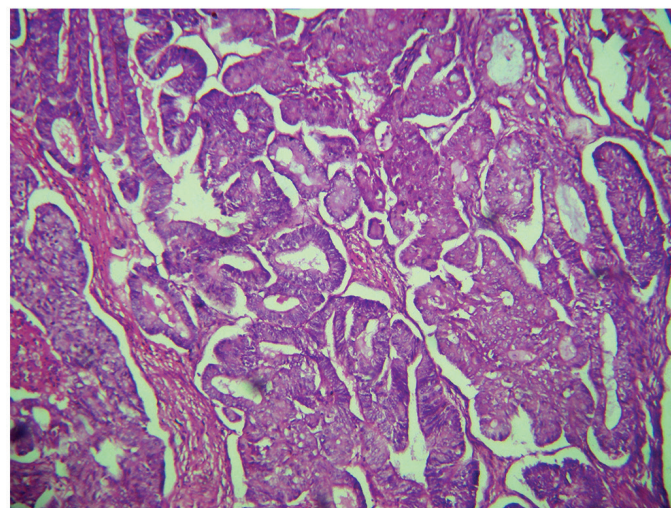
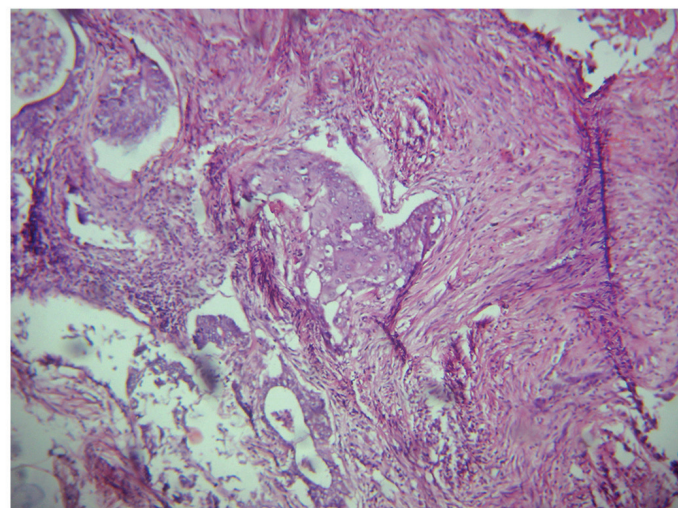
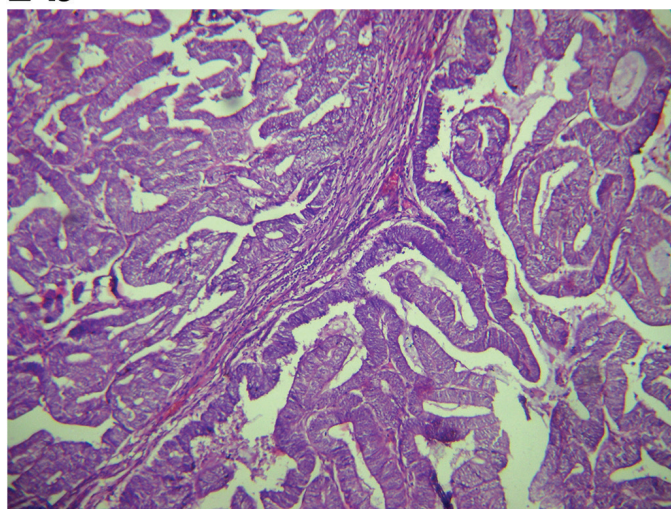
Endometrioid ovarian carcinomas comprise about 10-25% of all the primary ovarian carcinoma [5] and coexistent endometriosis can be demonstrated in 10-20% of the cases. In some cases the tumours can be seen arising from an endometriotic cyst [6]. However in this particular case there was no coexistent endometriosis or endometriotic cyst. Some patients with endometrioid carcinoma of the ovary have either endometrial hyperplasia or a synchronous endometrial adenocarcinoma [7]. In our case endometrial adenocarcinoma with metastasis to cervix was present.

Metastases from sites in the female genital tract to the ovaries can cause particular problems in differential diagnosis because synchronous primary tumors can occur and the histologic appearance of metastatic tumors can mimic that of primary ovarian carcinomas. Endometrial adenocarcinomas of endometrioid and serous types are the most common genital carcinomas to metastasize to the ovaries. Gross pathologic findings that suggest that the ovarian carcinoma might be metastatic include: the endometrial carcinoma is large and deeply invasive, the ovarian tumor is small, the ovarian tumor is multinodular and solid, the ovarian tumor is bilateral, surface implants are present on the ovary and extra-ovarian metastases are present in a distribution characteristic of

2 a



2 b

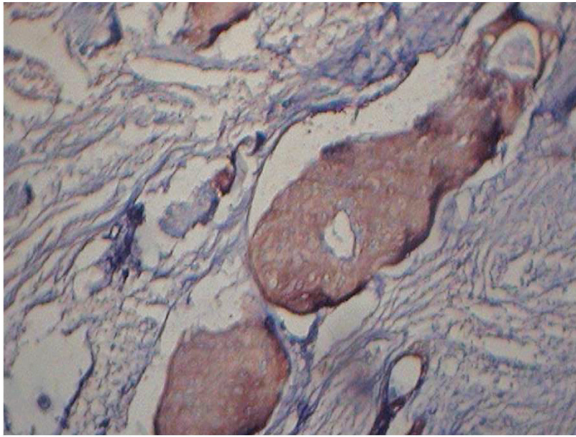


2 c

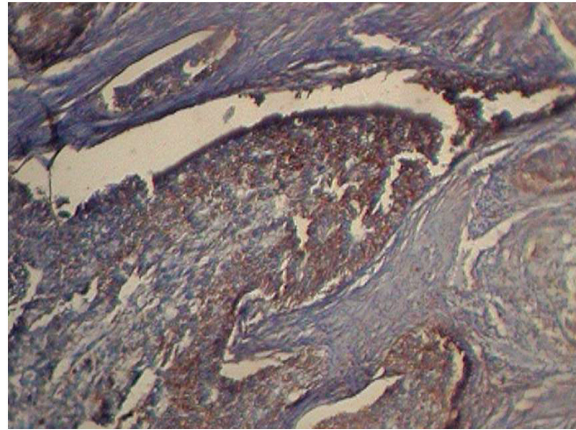
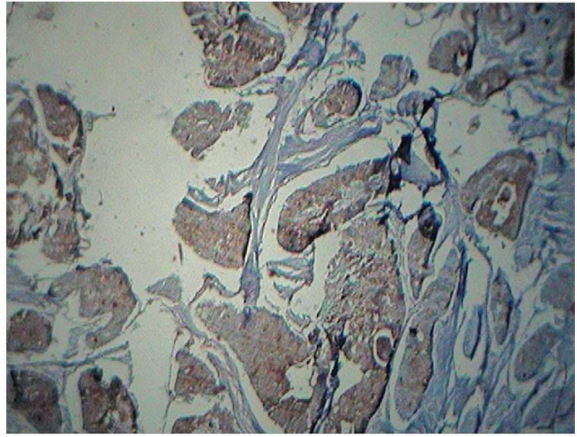
2 d

[Table/Fig 2a-d]: (a) Grade I endometrioid carcinoma with papillary change; (b & c) infiltration into myometrium and squamous differentiation

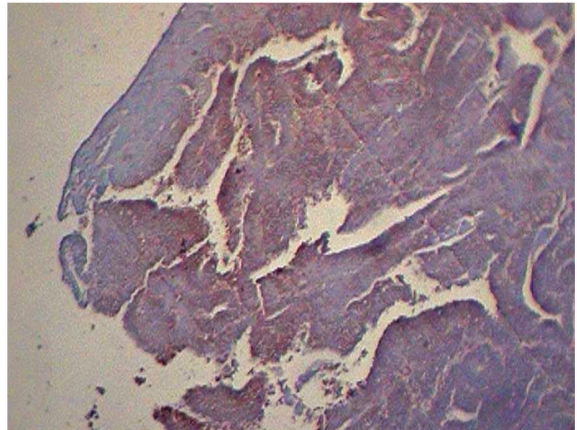
3 a



3 b



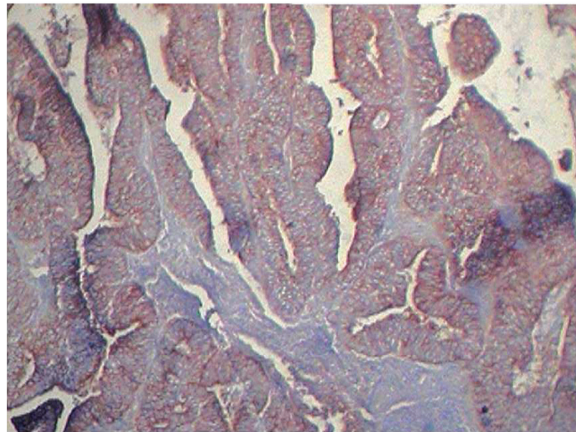
3 c



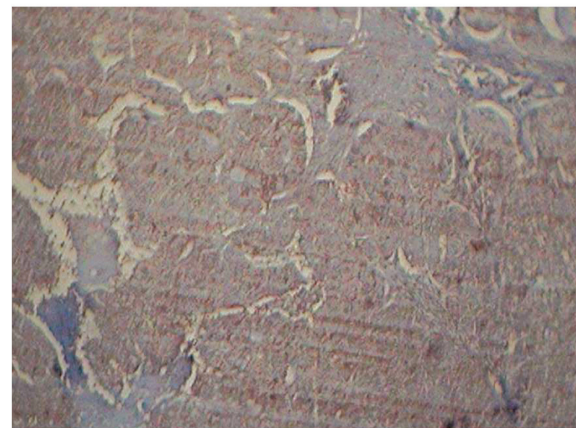
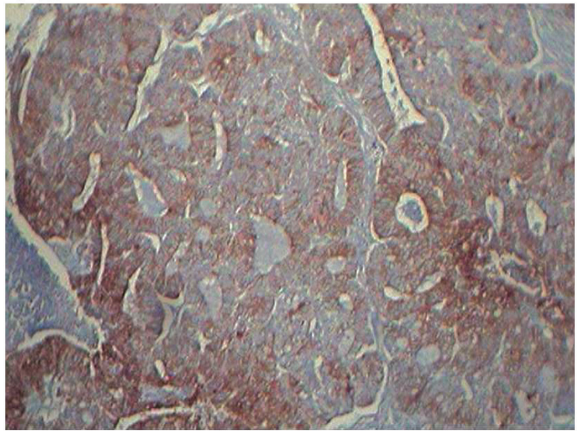
3 d

[Table/Fig 3]: Cytokeratin, EMA, and vimentin positive in the endometrium and vimentin positive in the cervix

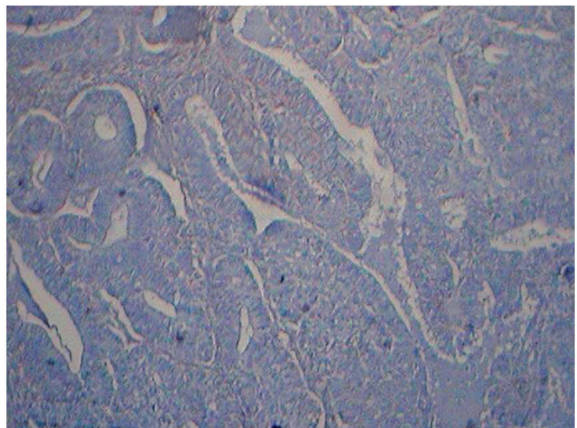
4 a



4 b



4 c



4 d

[Table/Fig 4]: Ovarian mass was positive for EMA and CK and negative for Vimentin

Test	Primary Endocervical	Primary Endometrial	Primary Ovarian
ER	Negative	Positive	Positive
PR	Negative	Positive	Positive
CEA	Strongly Positive	Weakly positive	Negative in endometrioid Positive in mucinous
Vimentin	Negative	Positive	Negative
CK7	Positive	Positive	Positive
EMA	Positive	Positive	Positive
P16	Positive	Negative	Negative
HPV in situ hybridization	Positive	Negative	Negative

[Table/Fig-5]: Immunohistochemical markers for distinguishing between primary endocervical, endometrial and ovarian tumours. (ER: Estrogen Receptor, PR: Progesterone Receptor, CEA: Carcinoembryonic Antigen, CK: Cytokeratin, EMA: Epithelial Membrane Antigen, HPV: Human Papilloma Virus)

endometrial adenocarcinoma (i.e., lymph node metastases more likely than peritoneal metastases) [8].

Several histologic features help to distinguish primary from metastatic tumours in the endometrium and ovaries. The presence of precancerous processes like endometrial hyperplasia or ovarian endometriosis is a strong evidence of in situ genesis. Different histologic types of synchronous endometrial and ovarian tumours are also good evidence of independent primaries. On the other hand similar histologic patterns cannot be taken as an evidence of metastasis as 15-20% of ovarian tumours with endometrioid histology are associated with histologically similar lesion in the endometrium.

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, 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].

In our case squamous differentiation was also noted with endometrial tumour. Search of literature showed that of all the endometrioid carcinoma of the endometrium, squamous differentiation is observed in 2-20% of cases and metastasis to the cervix is very common [10]. At the same time there was no squamous differentiation noted in cervical tumour, favouring metastasis of endometrial tumor to the cervix.

Ovarian endometrioid carcinomas are strongly immunoreactive for CK and EMA and negative for vimentin while endometrial primary tumour is positive for all three markers. Search of literature showed primary endometrioid carcinoma of the cervix is rare and they make about 7% of all the cervical adenocarcinomas. The possibility of primary endometrioid carcinoma of the cervix was excluded by immuno histochemistry. Primary endocervical tumours show a combination of carcinoembryonic antigen positivity and vimentin negative, while reverse is more characteristic of endometrial primary tumours. In our case primary endocervical tumour was ruled out as the cervical tumour was positive for vimentin [11].

Using International federation of Gynaecology and Obstetrics guidelines a patient diagnosed with dual primaries confined to the ovary and uterus represent two stage I cancers. These patients have good prognosis and depending on the substage may not require radio or chemotherapy. By contrast primary endometrioid ovarian carcinoma and endometrial metastasis would be stage IIA cancer and primary endometrial carcinoma with ovarian metastasis would be stage III A and require aggressive treatment [3].

To conclude it is necessary to identify synchronous primaries and metastatic tumours correctly as staging, prognosis and further management depend on it. In fact, standard criteria for differentiating between primary and metastatic tumors are likely to be misleading in this situation and additional testing is required. IHC and recently molecular diagnosis will provide the real confirmation. Immunohistochemistry plays an important role to differentiate single primary with metastasis and synchronous primaries especially at places with limited resources. The following IHC markers can be helpful in the differential diagnosis [Table/Fig-5] [12,13].

REFERENCES

- [1] Jaime P, Xavier M, José B. Simultaneous carcinoma involving the endometrium and the ovary. A clinicopathologic, immunohistochemical, and DNA flow cytometric study of 18 cases. *Cancer* 1991; 68 (11) 2455-2459.
- [2] Zaino RJ, Unger ER, Whitney C. Synchronous carcinomas of the uterine corpus and ovary. *Gynecol Oncol* 1984;19:329-35.
- [3] Momcilo D, Slobodanka M, Gordana D, Bozidar J. Endometrioid tumor of the ovary and uterus, metastasis or not – Case Report. *Acta Medica Medianae* 2007; 47(4):15-19.
- [4] Sadia H, Arif H, Janbazahmed. Coexistence of Endometrioid Adenocarcinoma of the ovary and the uterus. *Profesional Med J Mar* 2006; 13(1): 156-159.
- [5] Kline RC, Wharton JT, Atkinson EN, Burke TW, Gershenson DM, Edward CL. Endometrioid carcinoma of the ovary. Retrospective review of 145 cases. *Gynecol Oncol* 1990;39:337-346.
- [6] Mostoufizadeh M, Scully RE. Malignant tumours arising in endometriosis. *Clin Obstet Gynecol* 1980;23:951-963.
- [7] Czernobilsky B. Endometrioid neoplasm of ovary. A reappraisal. *Int J Gynecol Pathol* 1982;1:203-210.
- [8] Ulbright TM, Roth LM. Metastatic and independent cancers of the endometrium and ovary: a clinicopathologic study of 34 cases. *Hum Pathol*. 1985; 16:28-34.
- [9] Lee KR, Young RH. The distinction between primary and metastatic mucinous carcinomas of the ovary: gross and histologic findings in 50 cases. *Am J Surg Pathol*. 2003; 27:281-292.
- [10] Fletcher Diagnostic Histopathology of tumours volume – I Churchill publisher 2002 second edition p 658.
- [11] Richard RB, Maurie M et al., *Principles and practice of Gynecologic Oncology* Lippincott publisher 2009, Fifth edition p634
- [12] McCluggage WG, Sumathi VP, McBride HA, Patterson A. A panel of immunohistochemical stains, including carcinoembryonic antigen, vimentin, and estrogen receptor, aids the distinction between primary endometrial and endocervical adenocarcinomas. *Int J Gynecol Pathol*. 2002; 21:11-15.
- [13] Staebler A, Sherman ME, Zaino RJ, Ronnett BM. Hormone receptor immunohistochemistry and human papillomavirus in situ hybridization are useful for distinguishing endocervical and endometrial adenocarcinomas. *Am J Surg Pathol*. 2002; 26:998-1006.

AUTHOR(S):

1. Dr. Eswari V.
2. Dr. Geetha Prakash
3. Dr. Irfan A. Ansari
4. Dr. Bhanumathy V.
5. Dr. Gomathi Palvannanathan

PARTICULARS OF CONTRIBUTORS:

1. Corresponding Author.
2. Professor and Head, Department of Pathology, Meenakshi Medical College Hospital & Research Institute Enathur, Near Kanchipuram, Tamil Nadu.
3. Assistant Professor, Department of Pathology Meenakshi Medical College Hospital & Research Institute Enathur, Near Kanchipuram, Tamil Nadu.
4. Professor, Department of Pathology Meenakshi Medical College Hospital & Research Institute Enathur, Near Kanchipuram, Tamil Nadu.

5. Prof. & HOD, Department of Obs. & Gyneacology Meenakshi Medical College Hospital & Research Institute Enathur, Near Kanchipuram, Tamil Nadu.

NAME, ADDRESS, TELEPHONE, E-MAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Eswari V.

Assistant Professor, Dept. of Pathology

Meenakshi Medical College Hospital & Research Institute

Enathur, Near Kanchipuram, Tamil Nadu.

E-mail: dreswarimd@gmail.com.

Phone No. 9444510656.

DECLARATION ON COMPETING INTERESTS:

No competing Interests.

Date of Submission: **May 05, 2011**

Date of Peer Review: **Jul 03, 2011**

Date of Acceptance: **Jul 09, 2011**

Online First: **Jul 25, 2011**

Date of Publishing: **Aug 08, 2011**