Case Report

Triple independent primaries of female genital tract: A rare event

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ABSTRACT

The synchronous presence of endometrioid carcinoma of ovary and uterus in a single patient is an uncommon occurrence; but, finding a patient having a third simultaneous primary in cervix along with carcinoma ovary and endometrium is an extremely rare entity. In this article we describe a 40-year-old female who presented with gradual distension of abdomen, and underwent extended radical hysterectomy operation following diagnosis of an ovarian tumor on ultrasonography. On examination of the specimen, it was found to harbor endometrioid carcinoma of uterus and endometrioid carcinoma of ovary along with a small focus of well-differentiated squamous cell carcinoma of cervix. The presence of three coexistent primary tumors in female genital tract is an extremely rare event. Further molecular and genetic studies may throw light on the probable etiology of such rare cases.

Key words: Carcinoma, cervix, endometrioid, ovary, squamous, synchronous, uterus

INTRODUCTION

The simultaneous presence of carcinoma of the ovary and the uterus along with carcinoma cervix is a known entity, however, not so common. Endometrioid adenocarcinoma is found in the endometrium in 10% of women with ovarian endometrioid carcinoma.[1] The presence of endometrioid carcinoma in both endometrium and ovary may be either synchronous primary tumors in both uterus and ovary or metastasis of carcinoma from endometrium to ovary or vice versa.[2] But presence of three independent simultaneous primaries involving the ovary, uterus, and cervix is exceptional. This case is being reported because of its extreme rarity.

CASE REPORT

A 40-year-old multiparous female presented with chief complaints of gradual distension of abdomen for 1 month associated with vomiting and loss of appetite. Her past history was insignificant except low back pain 20 years back.

On ultrasonography of lower abdomen, uterus showed a heterogeneous hypoechoeic space occupying lesion (SOL) 1.7 × 1.2 cm at myometrium suggestive of fibroid, a left ovarian solid cystic SOL measuring 9.16 × 11.01 cm and ascitis [Figure 1].

Ascitic fluid was negative for malignant cells. Tumor marker CA 125 (318.2 U/ml), was raised, chest X-Ray showed a minimal pleural effusion.

The patient underwent an extended radical hysterectomy and the specimen was sent for pathological examination. On gross appearance, the uterus and cervix measured 8 × 5 × 4 cm. Uterine cavity was empty and endometrial thickness increased. Ovarian mass measured 15 × 10 × 6 cm. On cutting it revealed partly cystic and partly solid appearance with numerous papillary excrescences. Small papillary excrescences were also noted in cervix.

On microscopic examination of the uterus, proliferative endometrium with a small focus (about 3 mm) of well-differentiated endometrioid adenocarcinoma was seen, which did not penetrate in the deeper myometrium [Figure 2]. Cervix showed normal endocervical glands in continuity with a definite focus of well-differentiated keratinizing

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squamous cell carcinoma; the second primary [Figure 3]. Right ovary was of unremarkable morphology. Left ovary showed glands in round and cribriform architecture lined by atypical tall pseudostratified columnar epithelium and thus diagnosed as endometrioid adenocarcinoma [Figure 4]. The tumor was confined to the ovary without any extraovarian spread. Tubes were free from the tumor completely.

DISCUSSION

Dual primary carcinoma of female genital tract is an uncommon event. Therefore, our first challenge was to determine if the endometrioid carcinoma occurring in uterus and ovary were synchronous primary or one of them was metastatic. For this distinction we applied criteria as given by Ulbright and Roth. There is one major and five minor criterion to suggest that the ovarian carcinoma might be metastatic.[2]

Major criterion include: Multinodular ovarian involvement and minor criteria include: Small (<5 cm) ovarian size, bilateral ovarian involvement, deep myometrial invasion, vascular invasion, and tubal tumor involvement. At least one major and two minor criteria should be present.

Definitive information can be obtained from molecular diagnostic techniques. For example, PIK3, KRAS, and BRAF are commonly associated in multiple tumor-geneses in female genital tract.[3]

In our patient according to Ulbrights' criteria, both tumors were clearly primary as only one ovary was involved, size of the ovary was large (15 × 10 × 6 cm) that is more than 5 cm, tubes were uninvolved, deep myometrial invasion was absent in the uterine endometrioid adenocarcinoma, and there was no vascular or lymphatic invasion.

Thus both tumors of endometrium and ovaries were synchronous primaries. To add up with it, a cervical squamous cell carcinoma occurring at the same time in the same patient as a third independent primary of different histology is extremely rare event. Only one case report

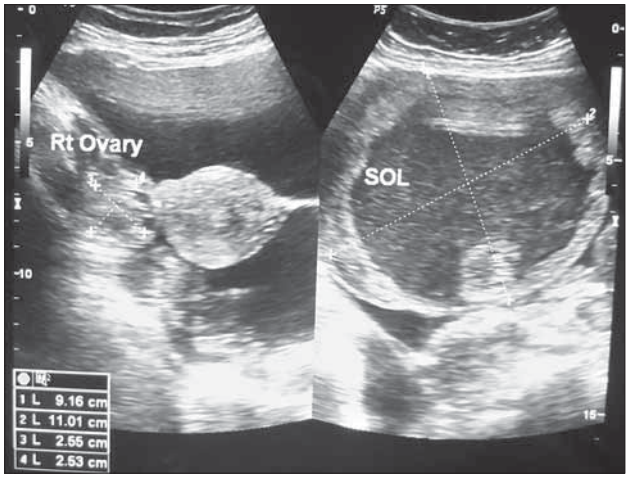

Figure 1: Ultrasonography of abdomen showing ovarian space occupying lesion

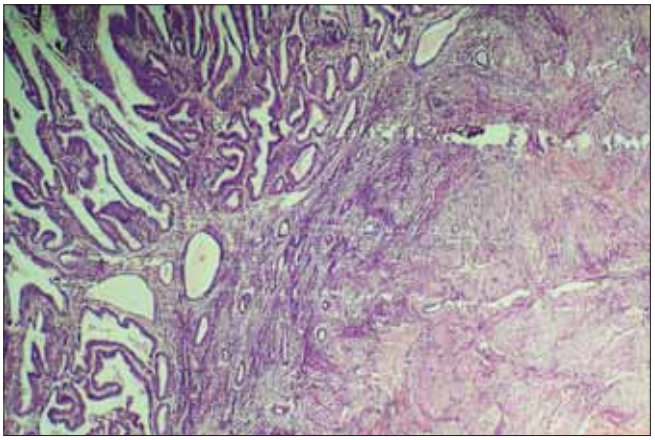

Figure 2: Photomicrograph of uterus showing endometrioid adenocarcinoma villoglandular type. Myometrium is free from invasion (H and E, ×100)

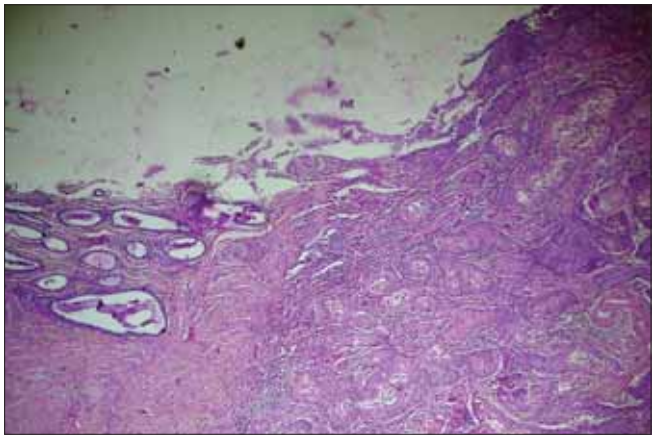

Figure 3: Photomicrograph of cervix showing normal endocervical glands in continuity with well differentiated keratinizing squamous cell carcinoma (H and E, ×40)

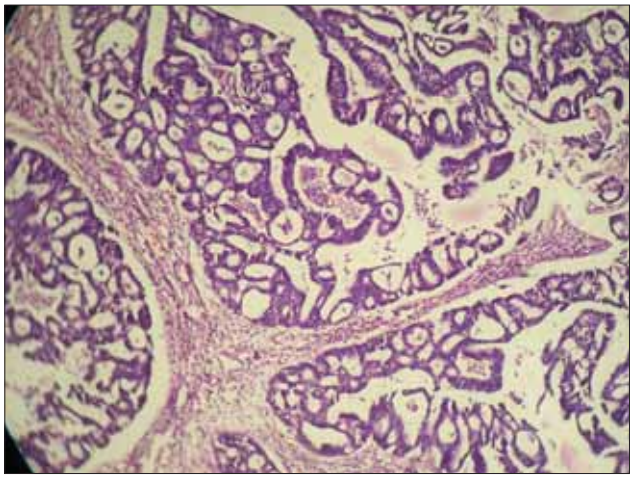

Figure 4: Photomicrograph of ovary showing endometrioid adenocarcinoma in cribriform pattern (H and E, ×100)

mentioning synchronous adenosquamous carcinoma of the endocervix, adenocarcinoma of the endometrium, low malignant potential of the right ovary, and mucinous cystadenocarcinoma of the left ovary has been reported.[4]

Scully further developed the Ulbrights' criteria to a more extensive degree.[3] On genetic analysis, various genes like PTEN, MMAC1, X-chromosome inactivation, and microsatellite instability have been found in these cases.[5-7] The pathogenesis of multiple primaries is unclear. As per the theory of secondary Mullerian system, the epithelia of cervix, uterus, fallopian tubes, ovaries, and peritoneal surface share molecular receptors responding to carcinogenic stimulus leading to the development of multiple primary malignancies synchronously.[8] In a study by Liu *et al*., synchronous primary endometrial and ovarian cancers are different from either primary endometrial carcinoma or ovarian cancer and are usually identified at early stages with a good prognosis.[9]

Our patient also presented at early stage and is fine till now. Further studies to find out the possible etiology, mechanism of oncogenesis, optimal treatment plans, methods of prevention, and early detection are needed. This will be an uphill task as such patients are seldom encountered.

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