

CASE REPORT

A Paragon Case of Double Synchronous Female Genital Malignancies- A Randevous of Ovarian Granulosa Cell Tumor with Uterine Endometroid Carcinoma: A Histopathological Case Report

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ABSTRACT

A granulosa cell or follicular cell is a somatic cell of the sex cord closely associated with oocyte development in females. The major function of granulosa cells includes the production of estrogen. Granulosa cells and ovarian epithelial cells develop from a precursor cell called a gonadal ridge epithelial-like cell. On the other hand, endometroid carcinoma or type I endometrial adenocarcinoma is one of the most common invasive cancers of the female genital tract in the world¹. Synchronous malignancies, including a dyad or more tumors of the genital tract, are rare². Herein, we present a case of a woman with concurrent simultaneous endometroid carcinoma and adult granulosa cell tumor of the right ovary, with discriminable histopathological characteristics.

Keywords: Synchronous tumors, granulosa cell tumor ovary, endometroid carcinoma, genital double cancer.

JMS: 2025; 28(3):11-14 DOI: <https://doi.org/10.33883/jms.v28i3.1438>

BACKGROUND

Synchronous primary tumors account for 0.7% -1.8% of all genital tumors. The most common synchronous primary tumors of the genital tract are ovarian and endometrial cancers. A retrospective observational study examining Surveillance, Epidemiology, and End Results Program (SEER) between 1973 and 2013, concluded that synchronous ovarian cancer has decreased among endometrial cancer, whereas synchronous endometrial cancer has increased among ovarian cancers. The differentiation of synchronous primary tumor from metastatic tumor is vital as it affects prognosis and management options. Here, we report two cases of anatomically related yet histologically unrelated tumors.

CASE PRESENTATION

A 55-year-old female underwent total abdominal hysterectomy with B/L salpingo-oophorectomy with lymph node removal for endometroid cancer, which had caused her

post-menopausal heavy P/V bleeding for 6months. On general examination, she was morbidly obese, with a long history of hypertension and diabetes mellitus of over 10 years. Her gestational history was G3P1A2L1. She reportedly had an early menarche at 9years of age and had her menopause at 48years. Based on a clinical diagnosis of endometrial cancer, confirmed by a positive biopsy, the patient underwent a total abdominal hysterectomy, B/L salpingo-oophorectomy, B/L pelvic and para-aortic lymphadenectomy.

On gross examination, the right ovary was markedly enlarged, measuring 7x4 x3 cm in size, with concomitant cystic areas ranging from 0.5x0.5cm to 1.5x1.5cm and a concurring solid portion of tumor. The affected ovary also showed tiny blood-filled cysts (figure 1a). On the cut section, greyish white to glittering yellow mass was seen,

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How to cite this article: Syed S, Shah S, Bhardwaj S, Ali S. A Paragon Case Of Double Synchronous Female Genital Malignancies. A Randevous Of Ovarian Granulosa Cell Tumor With Uterine Endometroid Carcinoma: JMS 2025; 28(3)11-14

Received: 2025-04-30 Accepted: 2025-08-29

Access this article online



Website:
www.jmsskims.org

DOI:
<https://doi.org/10.33883/jms.v28i3.1438>



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mirroring the lipid content of the same. The left ovary was grossly normal. The uterus was blatantly enlarged, measuring 12x10x7cm. Endometrial thickness was uneven, measuring 15 mm to 18mm at spots. A large exophytic friable mass distending the uterine cavity is seen in the endometrium of the fundus and right corpus of the uterus. The mass was papilliform at places to polypoid at the corpus, displaying a spectrum of colors ranging from dirty white to tan at places (figure 2a).

On HPE of the ovary, there were sheets of granulosa cells, admixed with theca cells and a few fibroblasts. The cells were arranged in diffuse and sarcomatoid patterns in most areas. There was increased nuclear pleomorphism and prominent nucleoli. In some areas, a gyriform pattern of arrangement was also seen. Typical Call Exner bodies were not observed. The presence of the characteristic pathognomonic coffee-bean nuclei was clear. Mitotic figures were present at 3-4/HPF.

The uterine sections showed increased proliferation of endometrial glands relative to the stroma, resulting in increased gland-to-stroma ratio. These glands simulated the physiological proliferative endometrium; hence the term endometrioid. Crowding of back-to-back budding and branching glands of various shapes, with scant intervening endometrial stroma, was seen. Colossal dilation of glands was well appreciated throughout the sections. The nuclei were markedly losing polarity and normal arrangement with the basement membrane, and exhibited a prominence of nucleoli and condensation of the nuclear membranes. Moreover, the endometrium was appreciably infiltrating into the myometrium, with characteristic paucity of stroma. The pushing endometrium showed 'papillary projections' at appreciable loci with a proper core of scant stroma with transgressing arborising network of capillaries. A sprinkling of infiltrating neutrophils was noted. There was a conspicuous element of squamous metaplasia with nesting of squamous cells. These showed the classic eosinophilic cytoplasm, bridging, and early keratin pearl formations. The mitotic figures were abundant, 4-5/HPF. Myometrial invasion was appreciated, but extending to less than 50% of the endo-myometrial junction. A microcystic, Elongated, and Fragmented (MELF) pattern of invasion of endometrial glands lined by flattened to histiocytoid epithelium was noted.

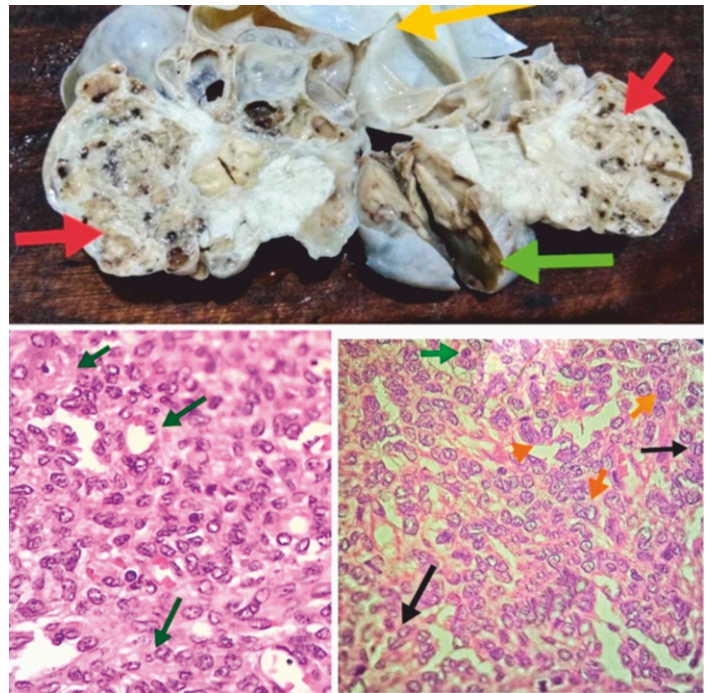


Fig 1: Gross examination of Granulosa cell tumor, adult type displaying a large unilateral cystic luteinized yellowish ovarian mass; with sheets of small cuboidal cells arranged in predominantly diffuse pattern with some foci of small follicle-like structures (black arrows) with angulated and grooved nuclei (red arrows) and occasional mitotic figures (green arrow).

DISCUSSION

Double cancers and multicentric cancers have been reported rarely until recently. Advances in diagnostics and an aging population have made them more recognized. A collision tumor is the true coexistence of two malignant neoplasms that are histologically different but found in the same organ or system³. Such tumors have components with different origins and develop as a mosaic of two simultaneous but distinct tumors. One hypothesis is that two primary tumors arise in continuity through an accidental meeting. Another is that the first tumor alters the microenvironment, which triggers the second adjacent tumor (ref4). Meyer classified such tumors as (a) collision tumors, (b) combination tumors, and (c) composition tumors. Thus, collision tumors are neighboring synchronous neoplasms that developed independently in the same organ or organ system.

Synchronous primary tumors of the genital tract are rare (2). Primary tumors of the ovary and endometrium have been

extrapolated to be the most common synchronous tumors of the female genital tract⁴.

Granulosa cells are sex cord somatic cells associated with the oocyte⁵. Majority of its function is the production of estrogen to help folliculogenesis. Granulosa cell tumors (GCT) are a type of sex cord-stromal tumor. They are the most common estrogenic ovarian tumors, constituting 5% of ovarian cancers⁶. It has two distinct histological types- adult GCT and juvenile GCT, which display different clinical and histopathological features. Adult GCTs are more common and seen in perimenopausal women, with a peak incidence at 50-55years. They constitute less than 5% of the ovarian tumors. Granulosa cell tumors are often hormonally active and associated with hyperestrogenism. Patients may present with vaginal bleeding due to endometrial hyperplasia or uterine cancer as a result of prolonged exposure to tumor-derived estrogen. About 25% GCTs develop a nasty recurrence with a median time of recurrence being 4-5years⁷; so regular follow-up and serum tumor markers like estradiol and inhibin are pretty reasonable. Histopathologically, Call-Exner bodies, which are rosetted follicular structures, often arranged in sheets, formed by granulosa cells with amorphous eosinophilic PAS+ve hyaline material in cores, are pathognomic and occur in 30 to 60% cases. Monotonous islands of granulosa cells with 'coffee-bean' nuclei constitute the bulk of the tumor section. The immunohistochemical panel includes inhibin, calretinin, and FOXL2.

Endometrioid adenocarcinoma was the commonest histology seen in endometrial cancers. Perhaps due to persistent hyperestrogenism in GST, endometrial pathology ranging from a polyp to endometrial hyperplasia and carcinoma has been documented⁸. Chronic estrogenic stimulation unopposed by progesterone affects glands to a greater extent than stroma, hence rendering the glandular hyperplasia. This is a precursor lesion for endometrioid carcinoma⁹. Estradiol is formed from androstenedione by the action of cytochrome P450 aromatase. Due to unregulated aromatase action, high levels of estrogen is seen in GST. Most frequently, it involves the uterine corpus. Primary cervical endometrioid adenocarcinomas are extraordinarily rare and likely develop from cervical endometriosis. Prognosis largely depends on FIGO/ TNM staging; however, age, tumor size, and histologic features

are also implicated. Positive stains include PAX8, CK7, ER/PR, and vimentin. Hysterectomy and bilateral salpingo-oophorectomy remain the primary treatment.

An autopsy series has reported that an increased prevalence of multiple primary cancers occurs in the same organ or in organs of the same system, like in our case, rather than in unrelated organs¹⁰.

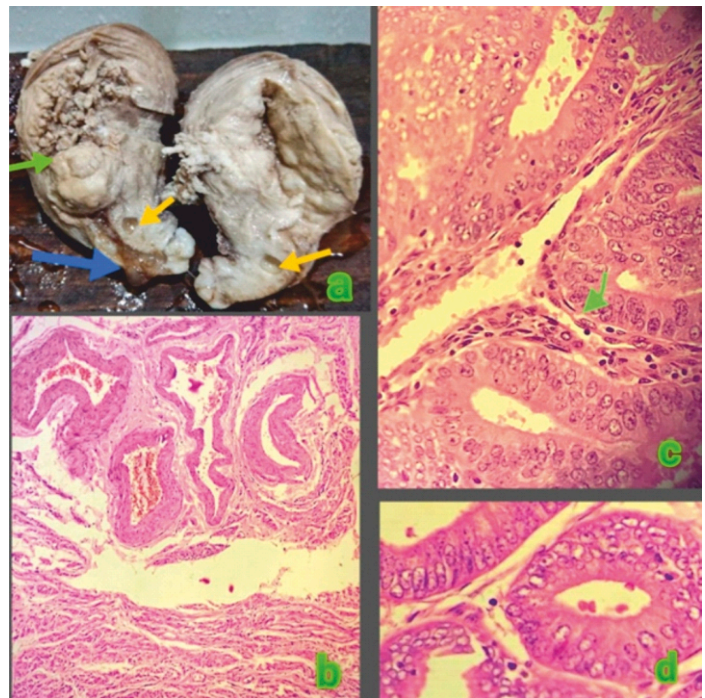


Fig 2: Gross examination of the enlarged uterus (a) with friable polypoid masses at the uterine corpus arising from endometrium and a broad based solid greyish mass arising in the body (green arrows) and cystic masses (yellow arrows) in lower segment near cervix (blue arrow) Histopathological pictures at low power (b) and high powers (c and d) of uterine sections showing endometrioid adenocarcinoma with glandular invasive (curved green arrow) pattern.

CONCLUSION

We conclude with deduction of the deduction that the coexistence of a lesion in anatomical proximity of a primary malignancy should not be labelled as metastasis, unless a thorough HPE evaluation is done; or else there is a good potential of omitting a concurrent synchronous primary malignancy, thereby perpetually risking patient prognosis & subsequent follow-up.

REFERENCES

1. Jhansivani Y, Rani S. Epidemiology of gynecological cancers in a tertiary care center(Government General Hospital, Guntur). 10SR J Dent Med Sci. 2015;14(9):41-5.
2. Axelrod JH, Fruchter R, Boyce JG. Multiple primaries among gynecologic malignancies. Gynecol Oncol 1984;18:359-72.
3. S. Warren and D. Gates, "Multiple primary malignant tumor: a survey of the literature and a stastical study"; American Journal of Cancer, Vol.51, pp.1358-1414, 1932.
4. Yao B, et al(2014) Aseries of collision tumors in genitourinary tract with a review of literature. Pathol Res Pract 210(4):217-223.
5. Zanagnolo V, Pasinetti B, et al. Clinical review of 63 cases of sex cord stromal tumors. Eur J Gynaecol Oncol 2004;25:431-8.
6. Young RH. Sex cord-stromal tumors of the ovary and testis; their similarities and differences with consideration of selected problems. Mod Pathol 2005;18(Suppl. 2):S81-89.
7. Zhang M, Cheung MK et al. Prognostic factors responsible for survival in sex cord stromal tumors of the ovary- an analysis of 376 women. Gynecol Oncol 2007;104:396-400.
8. Adamian RT. [Hyperplastic processes and endometrial cancers in patients with hormone producing ovarian tumors]. Vopr Onkol 1991;37:48-51.
9. Prefumo F et al . Epithelial abnormalities in cystic ovarian endometriosis. Gynecol Oncol 2002;84:280, Gyne
10. S. Watanabe, T. Kodama, Y. Shimosato et al. , "Multiple primary cancers in 5,456 autopsy cases in the: National Cancer Center of Japan", Journal of the National Cancer Institute, vol. 72, no. 5, pp. 1021-1027, 1984.