A Very Rare Occurrence of Synchronous Tumors of Variable Histology in Bilateral Ovaries

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ABSTRACT

Introduction: Ovarian tumors make up 30% of all cancers of the female genital system. Surface epithelial tumors of the ovary are by far the commonest variety (90%) followed by germ cell tumors (30%) and sex cord stromal tumors (8%). We present a case of a 46 year old female with bilateral ovarian mass showing two distinct histopathological types of ovarian tumor.

Case Report: A 46 year old female came with complaints of irregular menstrual cycles, abdominal pain and distension since 8 months. Serum CA125 level was elevated. Ultrasonography revealed a complex cyst arising from the left adnexa. Patient underwent staging laparotomy. Left ovary sent for frozen section which was reported as malignant was a solid and cystic mass measuring 14x12x6 cm with the inner surface showing a solid area measuring 10x10x5 cm. Right ovary measured 5x4.4x4 cm with a 4x4x4cm grey white solid area seen on the cut surface. Microscopy revealed a surprising histopathological picture of a clear cell carcinoma of the left ovary and a granulosa cell tumor of the right ovary which was confirmed by immunohistochemistry. Both the tumors were confined to the ovaries without lymph node involvement.

Conclusion: Morphologically different tumors arising from both ovaries is a rare occurrence with there being no case report of a synchronous clear cell carcinoma and granulosa cell tumor documented in literature.

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Introduction
Ovarian tumours make up 30% of all cancers of the female genital system. Surface epithelial tumours of the ovary are by far the commonest variety followed by germ cell tumours and sex cord stromal tumours.[^1,2] Mixed tumours of ovaries are well documented, however the occurrence of two distinct types of ovarian tumours in each of the ovaries is very rare and only few cases have been documented. We present a case of a 46-year-old female with bilateral ovarian mass showing two distinct histopathological types of ovarian tumor.

Case Report
A 46 year old female came with complaints of irregular menstrual cycles, abdominal pain and distention since 8 months. Serum CA125 level was elevated. Ultrasonography revealed a complex cyst arising from the left adnexa. Patient underwent staging laparotomy. Left ovary sent for frozen section had a solid and cystic mass measuring 14x12x6 cm with the inner surface showing a solid area measuring 10x10x5 cm.[Fig 1] Microscopy revealed a surprising histopathological picture of a cellular infiltrating lesion in the left ovary with solid, glandular and microcystic spaces lined by atypical tumour cells with clear cytoplasm and features of hobnailing corresponding to the histopathological picture of a clear cell adenocarcinoma.[Fig 3] Following this she underwent a trans abdominal hysterectomy with bilateral salpingo-oophrectomy and pelvic node dissection. Right ovary measured 5x4.4x4 cm with a 4x4x4 cm grey white solid area seen on the cut surface.[Fig 2] Histologically it showed a well-defined lesion consisting of monotonous population of tumour cells arranged in a trabecular pattern with scant eosinophilic cytoplasm and hyperchromatic nuclei with many cells showing nuclear grooving indicating a granulosa cell tumour.[Figs 6] Immunohistochemistry was done to confirm the diagnosis and to exclude the differential diagnosis of a mucinous adenocarcinoma. The clear cell adenocarcinoma was positive for cytokeratin 7[Fig 4], epithelial membrane antigen and negative for cytokeratin 20 with the background normal ovarian stroma showing positivity for WT-1.[Fig 5] Inhibin immune marker was done to confirm the diagnosis of a granulosa cell tumour which was diffusely and strongly positive. [Fig 7] Both the tumours were confined to the ovaries without lymph node involvement. Patient had no further management and was discharged. The patient is on regular follow up without any complications till date.

Discussion
The incidence of ovarian cancer is second only to uterine and cervical malignancies based on demographical locations.[^1,2] Factors responsible for the development of ovarian cancers include excessive estrogen, dietary habits and obesity.[^3,4] The tumor promoting role of estrogen in the development of ovarian cancers is of importance which acts through gene transcription causing cell proliferation and differentiation through the estrogen receptors and indirect free radical injury and mutation formation producing hormone metabolism.[^5] The role of mutations such as KRAS, BRAF in type-1 and p53 in type-2 ovarian cancers is of prognostic importance.[^5] Synchronous primary tumors if present in
Fig. 3: left ovary (H&E): Clear cells with nuclear atypia and hobnailing.

Fig. 4: left ovary: Tumor cells positive for cytokeratin 7.

Fig. 5: left ovary: Tumor cells negative for WT-1 with the background stroma showing nuclear positivity.

Fig. 6: right ovary (H&E): Tumor cells with features of nuclear grooving.

Fig. 7: right ovary: Tumor cells positive for inhibin.
the female genital tract is usually seen in the age group of 25-45 years with the most common being an endometrial adenocarcinoma and a surface epithelial ovarian carcinoma. Primary synchronous ovarian tumors of variable histology is a rare presentation with occasional case reports of a serous carcinoma and clear cell adenocarcinoma and a mature teratoma with a mucinous cystadenoma. Our case presented with a clear cell carcinoma of the left ovary and a surprising incidental finding of a granulosa cell tumor in the right ovary. Clear cell adenocarcinoma is a malignant tumor which is classified under the surface epithelial tumors of the ovary. Macroscopically the lesion has a mean size of 15 cm and may have a unilocular or multiloculated cyst with solid and fleshy nodules. These tumors arise from an endometriotic cyst and may contain chocolate brown fluid. Microscopically the tumor cells are polygonal with abundant clear cytoplasm arranged in sheets or forms the lining of tubulocystic or papillary structures showing features of hobnailing separated by a fibrovascular or hyalinised stroma. Clear cell adenocarcinomas are high grade tumors with poor prognosis. Granulosa cell tumor which is classified under the sex cord-stromal tumors which are composed of granulosa cells in a fibrothecomatous background. They are further subtyped into adult and juvenile granulosa cell tumors based on the age of presentation and cytological features. The histological picture is that of tumor cells arranged in variety of patterns with scant cytoplasm, round to oval nucleus with a nuclear groove along with the typical Call-Exner bodies. The tumors are hormonally active and can also have atypical clinical presentations and morphology. Granulosa cell tumors have potential for recurrence and the most important prognostic factor is the stage of the tumor. In our case the grading and staging of both the ovarian tumors was done according to the AJCC/UICC TNM, 7th edition, and FIGO 2014. Immunohistochemistry for clear cell carcinoma of the ovary shows positivity for keratins, CA125 and hormone receptors while granulosa cell is positive for inhibin and calretinin.

Conclusion
We document the rare synchronous occurrences of clear cell carcinoma in the left ovary and incidentally detected granulosa cell tumour of the right ovary. This case is documented to highlight the fact that histologically diverse tumours can occur in the ovaries and immunohistochemistry is proven useful in distinguishing them.

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Competing Interests
None Declared

Reference


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