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Case Report

Synchronous ovarian granulosa cell tumor and carcinoma endometrium due to excess estrogen secretion: a rare presentation

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ABSTRACT

Granulosa cell tumor (GCT) is a low malignant potential ovarian tumor accounting for 70% of all sex cord stromal tumor. It is an estrogen secreting tumor, hence diagnosed in early stages, associated with 20-30% concomitant lesion in endometrium including 5% of invasive adenocarcinoma. Through this case report we present the synchronous occurrence of ovarian and endometrial malignancy of a 52-year-old female, P3L2A0 who presented with irregular menstrual bleeding since 2 months along with literature review. Imaging showed endometrial lesion with synchronous left ovarian lesion with a normal CA-125. Underwent total abdominal hysterectomy with bilateral salphingo-oophorectomy and post op histopathology showed FIGO stage IC GCT of left ovary and Endometrioid carcinoma of endometrium, grade1, FIGO stage IA, low risk with P-53 negative by IHC. In view of ovarian tumor FIGO stage IC GCT, she received adjuvant chemotherapy. Hence, presence of synchronous endometrial lesion with suspicious ovarian mass at presentation should suspect the diagnosis of estrogen secreting GCT with endometrial lesion.

Keywords: Synchronous, Granulosa cell tumor, endometrium carcinoma, Estrogen

INTRODUCTION

Granulosa cell tumor (GCT) is an ovarian tumor with low malignant potential derived from non-germinal elements of ovarian tissue. It is an uncommon tumor of ovary, accounting for 70% of all sex cord stromal tumors.[1-4] Menopausal and postmenopausal women are more prone for granulosa cell tumor than reproductive age group.[3] These tumors have specific biologic function of elaboration of estrogenic hormone causing the growth of those organs which are physiologically responsive to estrogen such as endometrium and breast.[5] Due to estrogen secretion, these are usually diagnosed in early stages and lower grade.[6,7] It is associated with 20-30% concomitant lesion in endometrium rarely 5% of invasive adenocarcinoma.[2,3,8] Two histological forms occur, which includes adult and juvenile form. These juvenile form presents with pseudo puberty (50%) and galactorrhea.[9]

Whenever there is a preoperative imaging with ovary and endometrial lesion should have the high index of suspicion, then only a occurrence of synchronous malignancy will be diagnosed upfront and these images are also useful in planning the optimal surgery and further decision on adjuvant therapy.[3] Histopathological assessment and confirmation with immunohistochemistry is an important step for diagnosing, grading, staging and risk assessment for deciding further treatment.[10] In cases of high risk of recurrence in GCT, platinum-based adjuvant chemotherapy is recommended, similar to epithelial carcinoma of ovary from stage IC onward.[11] Five-year survival of GCT with or without associated endometrial lesion approaches to 97%- and 20-year survival rate of 66.8%. GCT are associated with late recurrences requiring long term follow up of these patients.[9] Synchronous granulosa cell tumor and carcinoma endometrium is rare.[3]

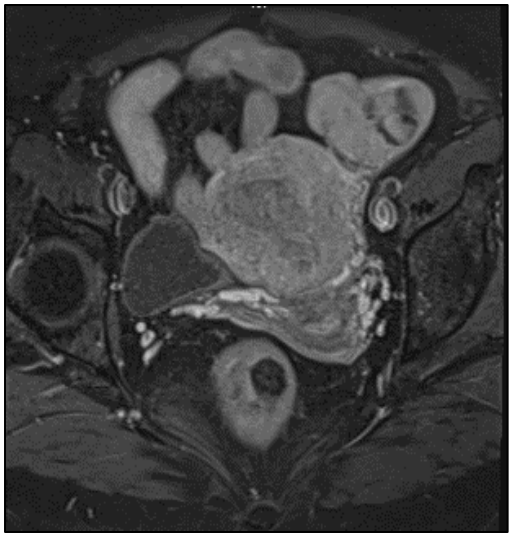

Figure 1: MRI-T1w of pelvis with contrast-showing heterogeneously enhancing endometrial and left ovarian lesion.

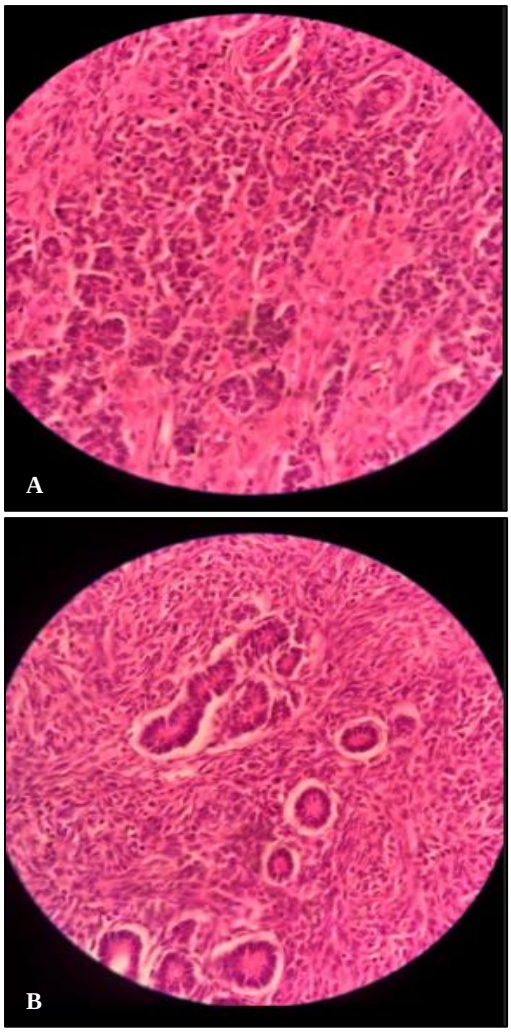

Figure 2 (A and B): Histopathological images showing call Exner bodies in low and high-power view seen in granulose cell tumor ovary.

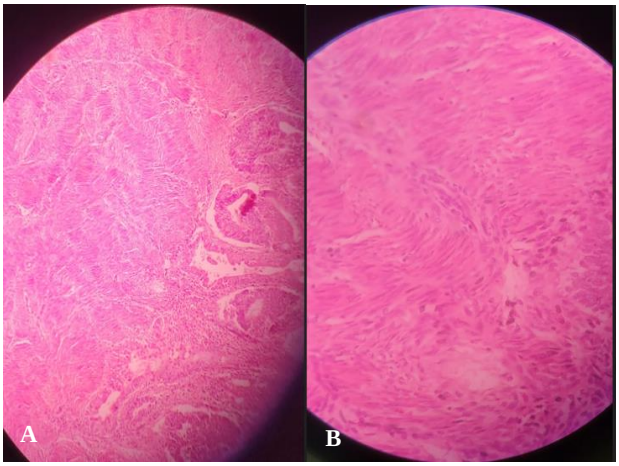

Figure 3 (A and B): Histopathological images showing endometrial adenocarcinoma under low and high-power view.

Synchronous dual malignancies are to be managed considering both the sites risk factors stage, grade and other prognostic and predictive factors for determining the requirement of adjuvant therapy. In this case report we present the synchronous occurrence of ovarian and endometrial malignancy of a 52-year-old female, P3L2A0, who presented with irregular menstrual bleeding since, 2 months along with literature review of last 15 years of the same.

CASE REPORT

52-year-old female, P3L2A0 came with complaints of Irregular menstrual bleeding since, 2 months. MRI abdomen and pelvis was suggestive of endometrial lesion infiltrating <50 % of the myometrium with synchronous left ovarian lesion with a normal CA-125 (10.7 IU/Ml).

She underwent total abdominal hysterectomy with bilateral salpingo-oophorectomy for the same and post operative histopathology showed FIGO stage IC GCT of left ovary with surface deposits and Endometrioid carcinoma of endometrium, grade 1 FIGO stage IA, low risk with TP53 negativity by IHC.

Postoperative inhibin A and inhibin B levels were normal (not done at presentation as GCT was not suspected upfront) and Postoperative PETCT scan showed no focal hypermetabolic or enhancing lesion. After discussion in multidisciplinary tumor board patient received adjuvant treatment of 3 weekly, 6 cycle inj paclitaxel 175 mg/m2 and inj carboplatin AUC 5 as indicated for FIGO stage IC GCT and observation for endometrium. Presently patient is on regular follow up, at 6 months patient is clinically stable and tumor marker levels are with in normal limits.

Literature review of synchronous granulosa cell tumor of ovary and carcinoma endometrium in mentioned in the table 1 and 2 as case series and case reports respectively.

We present three case series in Granulosa cell tumor with synchronous endometrial lesion, with number of patients ranging from three to twenty-eight and had minimum age of 33 years and maximum age of 72 years.[1,5,9] Median age of 53 years with majority in fifth or sixth decade. The common presenting symptoms were vaginal bleeding and abdominal pain with 14 cm mean tumor size. Granulosa cell tumor is usually of adult and juvenile histological subtypes, former type is often diagnosed in an early stage of disease and are associated with slow clinical progression. Most patients presented with abdominal pain (59%), vaginal bleeding (59%), abdominal distension (44%), menstrual bleeding (37%), postmenopausal bleeding (19%) and amenorrhea (11%).[9]

Most patients included in the three-case series were invasive carcinoma of endometrium with granulosa cell tumor. Only 6 patients presented with synchronous benign lesion of endometrial hyperplasia.[9] Majority underwent surgery with six patients received adjuvant chemotherapy or radiation in one case series by Antolic et al, indicating the early stage of disease presentation (63%).[1,9] These cases had maximum follow up upto nine years with most patients being disease free.[5] Late recurrences are common, requiring prolonged follow up of patients mainly for adult type of histology. Five- and nine-year overall survival were 91.3% and 77.3% respectively.[9] In this report we also present case reports of granulosa cell tumor with synchronous endometrial lesion in the last 15 years. We found around eleven relevant case reports. Median age of presentation among these case reports was 65 years with 82% (9 patients) being postmenopausal. Surgery was the primary treatment in majority of patients and only two patient received adjuvant chemotherapy due to risk factor of recurrence.[11,12]

All patients were disease free at the reporting follow up time period of each case reports which varied from 10 days to 34 months, insisting the requirement longer follow up. In one report analysis of p53 was also done as predictive marker for the treatment in both ovarian granulosa cell tumor and endometrial lesion.[7] Synchronous presentation of granulosa cell tumor and endometrial lesion have better prognosis due to early-stage diagnosis and lower grade, not requiring any adjuvant treatment.[13]

Table 1: Literature review of case series in granulosa cell tumor with synchronous endometrial lesion.

Case series						
S. No.	**Year of publication**	**Number of patients**	**Age (in years)**	**Invasive disease/benign endometrial disease**	**Treatment received**	**Outcomes**
1	1942[5]	3	42 to 64 yrs	Invasive disease	Surgery	Maximum of 9 yr FU-stable
2	1980[1]	28	33 to 72 yrs	Invasive disease- 8%	Surgery mainly RT/CT in 6 patients	Alive upto -9 yrs
3	2013[9]	27	Mean age 53 yrs	6 patients had endometrial hyperplasia	Surgery	Median FU 63 months 18.5% relapse and 4 died due to disease

Table 2: Literature review of case reports of granulosa cell tumor with synchronous endometrial lesion in the last 15 years.

S. No	Year of publication	Menopausal status (Post menopausal=*)	Age (in years)	Treatment received	Outcomes (FU- follow up)
1	2023[11]	*	58	Surgery and adjuvant chemotherapy	10 months FU, clinically stable
2	2022[17]	*	65	Surgery	-
3	2022[16]	*	65	Surgery	2-month FU, normal
4	2020[12]	*	50	Surgery and adjuvant chemotherapy	34 months FU, disease free
5	2018[8]	*	80	Surgery	2 years FU, normal
6	2018[14]	Menstruating	45	Surgery	-
7	2018[10]	*	85	Surgery	5 months FU, no disease
8	2015[4]	*	65	Surgery	2 years FU, disease free
9	2011[15]	Menstruating	35	Surgery	-
10	2011[3]	*	65	Surgery	10 days post discharge, normal
11	2010[13]	*	73	Surgery	-

DISCUSSION

Granulosa cell tumor constitutes for 5% of all ovarian malignancies and most commonly seen in postmenopausal women.[14] Median age of presentation is 50-55 years.[9] Commonly seen in premenarcheal or postmenopausal period than in the reproductive period, as it is associated with excess estrogen.[1] GCT are of two types: adult type and infantile type.

Adult type is more common with good prognosis and late recurrence.[9] Histopathologically it is characteristic of call exner bodies and on immunohistochemistry it expresses vimentin, inhibin, calretinin, and CD56.[15] Granulosa cell tumor is an estrogen secreting tumor, hence diagnosed in early stages.[6] Inhibin A and Inhibin B are serum tumor marker specific for GCT. Few genetic diseases like Ollier disease and Peutz-Jeghers syndrome are at higher risk of sex-cord stromal tumor.[15]

Most of the GCT are diagnosed in the post operatively.[16] Ninety percent of sex cord tumor is granulosa cell tumor.17 It is also associated with 20-30% concomitant lesion in endometrium including 5% of invasive adenocarcinoma due to estrogen secretion and also associated with increased risk of carcinoma breast.8 Synchronous occurrence of two primary gynaecological tumors are usually seen in elderly, overweight women with history of hypertension and diabetes mellitus, postmenopausal and multiparous women.

Synchronous ovary and endometrium malignancies have a better outcome due to the low-grade histology and early stages of diagnosis.[13] Synchronous dual malignancies are to be managed considering both the sites individually. Surgery is the main modality of treatment for both GCT and carcinoma endometrium.[9]

GCT with Stage IC and above stage are recommended for adjuvant chemotherapy.[2] Molecular subtyping in early stage of endometrium identifies the risk for the need of adjuvant therapy. GCT requires long term follow up as it is associated with late recurences.[9,8]

CONCLUSION

Presence of synchronous endometrial lesion with suspicious ovarian mass on imaging should suspect the diagnosis of estrogen secreting GCT with endometrial lesion. Upfront measurement of Inhibin level to be considered in all suspected cases of GCT. At least testing for TP53 and POLE mutation for predicting the risk in carcinoma endometrium to be considered in all cases for deciding adjuvant treatment in early-stage disease in Indian settings.

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