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CASE STUDY

A CASE OF SYNCHRONOUS GRANULOSA CELL TUMOR OVARY WITH ENDOMETRIAL CARCINOMA – A RARE CASE REPORT WITH REVIEW OF LITERATURE

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ABSTRACT

Granulosa cell tumors (GCT) are rare tumors of the ovary, arising from sex cord stromal cells and account for 3-5% of all ovarian tumors. These tumors were first described by Rokitansky. There are 2 types- adult variety and juvenile variety. Adult GCTs are 95% of total GCTs and are most commonly found in age group of 50-55 years. Juvenile GCTs are rare tumors occurring in young girls usually before menarche and account for 5% of all GCTs. These are functional tumors which secrete estradiol which leads to various manifestations like isosexual precocious pseudopuberty in juvenile type and abnormal vaginal bleeding (menometrorrhagia) in perimenopausal & postmenopausal women in adult types. Due to prolonged hyperestrogenic state, there is evidence of endometrial hyperplasia leading to well differentiated endometrial carcinoma in 5 % of patients. We are reporting case of an 80 years postmenopausal female with moderately differentiated endometrioid adenocarcinoma endometrium with less than 50% myometrial invasion with stage 1A granulosa cell tumor of left ovary in final histopathology post surgery. These tumors have different biology and clinical presentation than that of epithelial ovarian cancers that are stage III at diagnosis in most of the cases. Most of GCTs are stage I at diagnosis (80-90%). There is delayed recurrence potential in these tumors. There are 4 times increased risk of developing breast cancer as well as due to hyperestrogenic state. There are very few cases of synchronous GCT and endometrial carcinoma in literature and with best of our knowledge, no such case has been reported from India.

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INTRODUCTION

Granulosa cell tumors (GCT) are rare tumors of the ovary, arising from sex cord stromal cells and account for 3-5% of all ovarian tumors (Fox *et al*., 1975). Epithelial ovarian tumors followed by germ cell tumors are common ovarian tumors. These tumors were first described by Rokitansky. There are 2 types- adult variety and juvenile variety. Adult GCTs are 95% of total GCTs and are most commonly found in age group of 50-55 years. Juvenile GCTs are rare tumors occurring in young girls usually before menarche and account for 5% of all GCTs (Fox, 1975). These are functional tumors which secrete estradiol which leads to various manifestations like isosexual precocious pseudo puberty in juvenile type and abnormal vaginal bleeding (menometrorrhagia) in perimenopausal and postmenopausal women in adult types.

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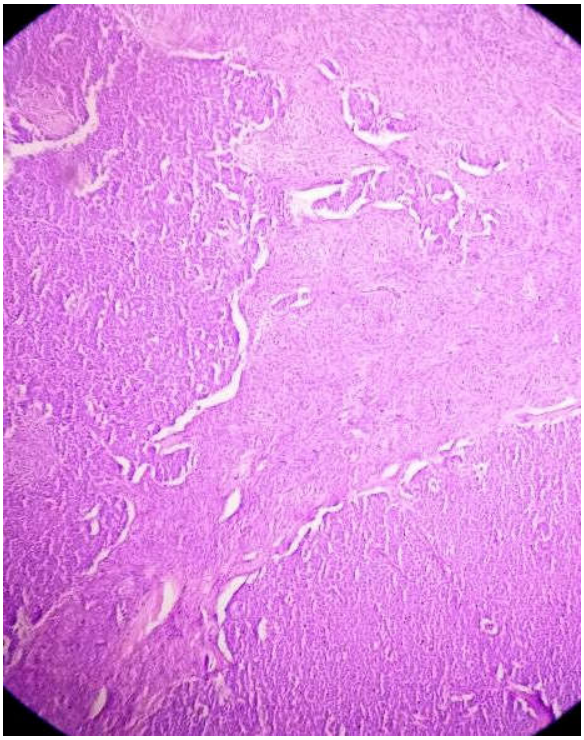
Due to prolonged hyper estrogenic state, there is evidence of endometrial hyperplasia leading to well differentiated endometrial carcinoma in 5 % of patients (Evans, 1980).

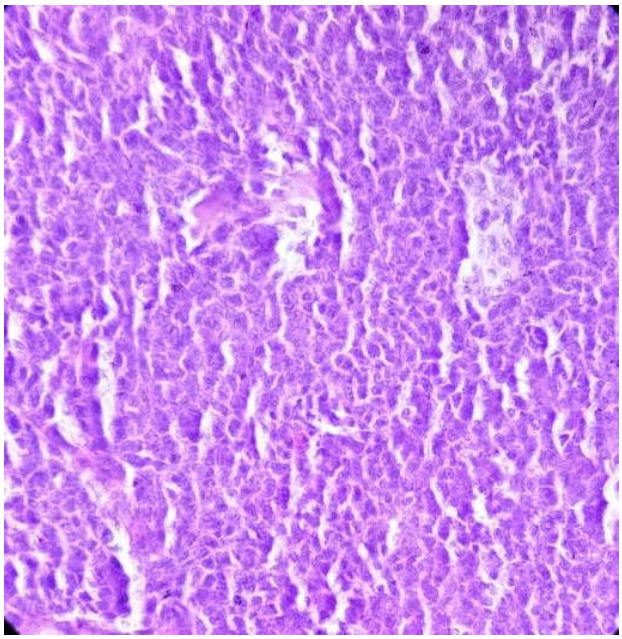
Case report

80 years postmenopausal female with H/O diabetes and hypertension presented to us with complaint of pain lower abdomen since 3 months and bleeding per vaginum since 1 year. She was evaluated with CT abdomen which showed left sided complex solid cystic ovarian mass of size 5×3 cm merging with myometrium. There was bulky uterus with endometrial hyperplasia. CT thorax was normal. She underwent examination under anaesthesia (EUA), dilatation and curettage (DandC) and cervical biopsy on 2.2.16. Endometrial biopsy was S/O endometrioid adenocarcinoma while cervical biopsy was S/O chronic cervicitis. Her preoperative CA125 level was 0.9 mIU/ml, AFP level was 11.0

ng/ml and beta hCG level was 2.3 mIU/ml. She underwent staging laparotomy with TAH+BSO with pelvic and paraaortic lymph node dissection on 11.2.16.

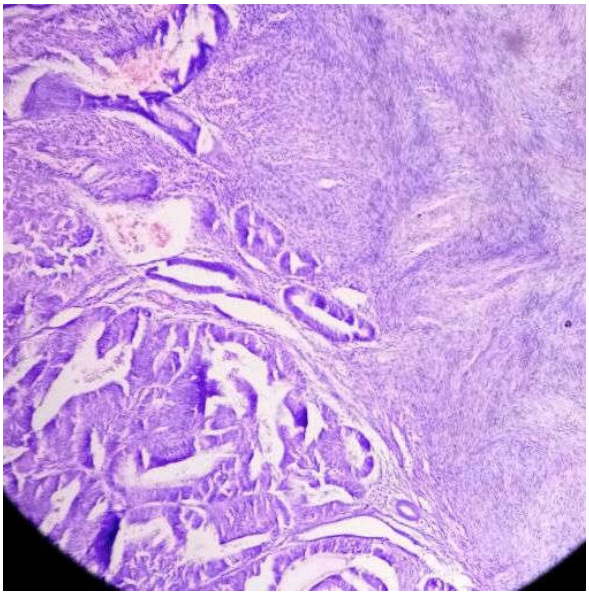


1A-ovary showing tumor with expansile pattern arranged in sheets and nests (10X, H+E)

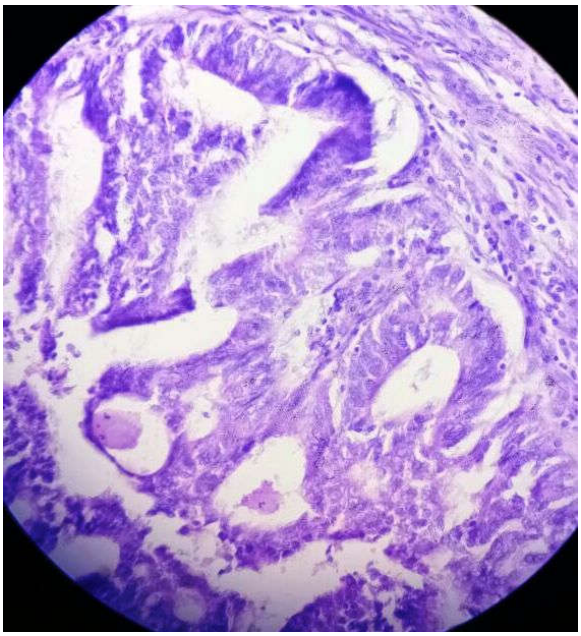


1B-monomorphic tumor cells with vescicular nuclei, conspicuous nucleoli (40X, H+E)

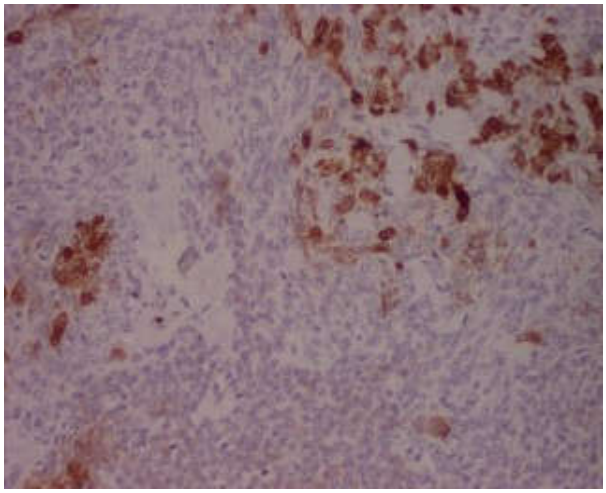
Final histopathology was S/O moderately differentiated endometrioid adenocarcinoma endometrium with less than 50% myometrial invasion with stage 1A granulosa cell tumor of left ovary (Figures 1A, B, C, D). It was subsequently confirmed by immunohistochemistry with positivity for inhibin (Figures 2A,B,C,D). Patient subsequently received 3 sessions of high dose rate vaginal brachytherapy in dose of 7Gy each fraction till April 2016. She is on regular follow up since then and is disease free till her last visit in April 2018.

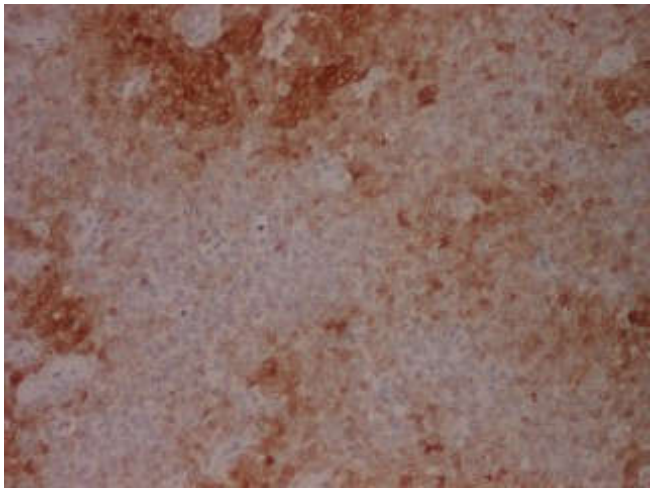


1C-uterine corpus showing an invasive endometrioid adenocarcinoma arranged in complex glandular pattern (10X, H+E)

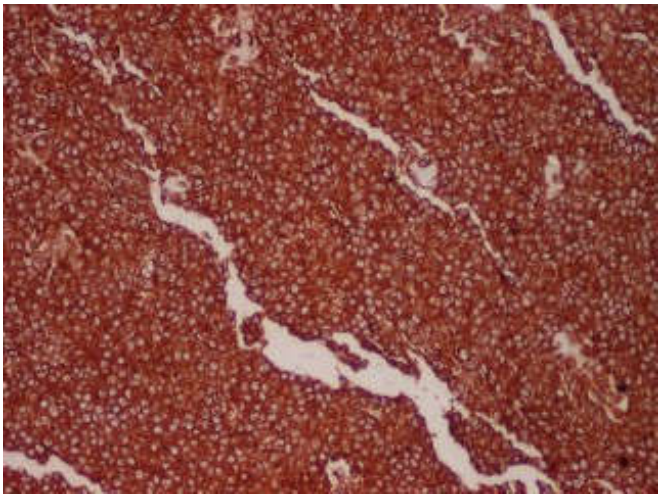


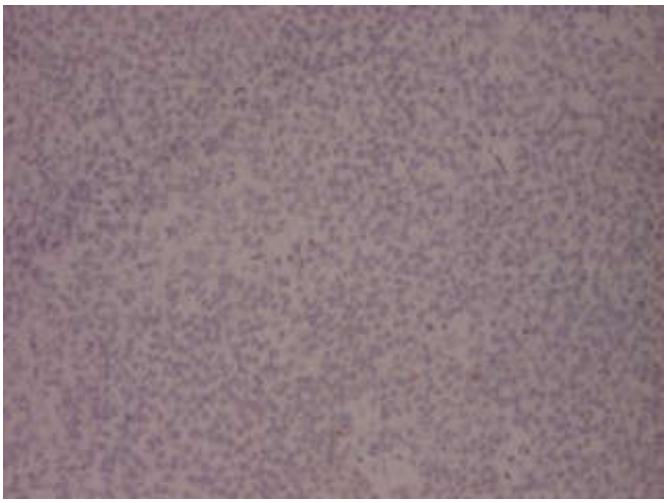
1D- uterine corpus showing an invasive endometrioid adenocarcinoma arranged in complex glandular pattern (40X, H+E)





2A-IHC stain for inhibin
2B-IHC stain for calretinin





2C-IHC stain for vimentin
2D-IHC stain for CK

DISCUSSION

Granulosa cell tumors are rare neoplasms of ovary which are functional and secrete estrogen leading to various clinical manifestations. These tumors have different biology and clinical presentation than that of epithelial ovarian cancers that are stage III at diagnosis in most of the cases (Evans, 1980). Most of GCTs are stage I at diagnosis (80-90%). GCT and thecoma, both are estrogen secreting tumors and are collectively called as feminising mesenchymomas of ovary (Evans, 1980).

Tumor markers for GCT are serum estradiol, inhibin, follicle regulatory protein and mullerian inhibitory substance (Koukourakis *et al*., 2008). Although estradiol has been labelled as tumor marker for GCT but its levels don't have direct concordance with size or tumor load. Most of these patients will have endometrial hyperplasia (30-85%) and only 5% will develop concurrent well differentiated endometrial carcinoma (Evans, 1980; Koukourakis *et al*., 2008). Endometrial carcinoma has been divided into 2 types. Type 1 account for 80 % of cases and are associated with hyperestrogenic state, early diagnosis and good prognosis. Type 2 tumors are non estrogen dependent, very rarely associated with GCTs, are mostly associated with TP53 mutation and have poor prognosis. Very rarely it is associated with serous carcinoma endometrium but in these cases, TP53 mutation is usually associated (Talhouk *et al*., 2016).

Workup should include CT abdomen, chest imaging and tumor markers like serum CA125, LDH, alfa fetoprotein, hCG, inhibin and estradiol. CT may show solid to solid cystic multilocular masses with endometrial hyperplasia in most of the patients. Advanced cases may show ascites, peritoneal deposits, lymphadenopathy etc (Pectasides, 2007). Surgery is treatment of choice in resectable tumors. TAH + BSO with pelvic and paraaortic lymph node dissection as per classical ovarian laparotomy is standard. Unilateral salpingectomy has been done in few younger patients less than 40 years with normal appearing endometrium who are keen for fertility preservation. It carries higher recurrence rates and the risk should be explained before going for fertility preservation surgery. In these patients, endometrial curettage is must, to rule out early endometrial carcinoma within endometrial hyperplasia (Koukourakis *et al*., 2008).

Pathologically GCT may show various levels of differentiation and patterns like micro follicular, trabecular, tubular, solid and water silk patterns. Nuclear grooving and Call Exner bodies are characteristically seen in GCTs (Evans, 1980; Koukourakis *et al*., 2008; Koukourakis *et al*., 2008). Stage is most important prognostic factor. The survival rates at 10 years are 90% in stage I, 50-60% in stage II and 17-33% in stage III-IV (Savage, 1998; Björkholm, 1981). Age less than 50 years has been found as good prognostic factor by Zhang *et al* but contrasting results has been seen in some studies (Zhang *et al*., 2007). Similarly ruptured tumor capsule, positive cytology, residual disease post surgery, bilateral disease and ascites are associated with poor results in some reports but robust data is lacking considering rarity of tumor and delayed recurrence potential. There are 4 times increased risk of developing breast cancer as well as due to hyperestrogenic state (Ohel, 1983). In stage I tumors, surgery alone is sufficient. In more advanced tumors, chemotherapy should be given. We can use either BEP based chemotherapy or other platinum combination regimen. The role of adjuvant radiation has been conflicting because in some reports, it has shown to reduce mortality, while in others, no effect has been seen however it is difficult to interpret in the absence of randomised trials. The chances of recurrence are mostly within 10 years after treatment but reports have shown delayed recurrence even after 40 years after surgery (Fujita, 2015). So every patient of GCT irrespective of age or stage should be followed indefinitely. There are very few cases of synchronous GCT and endometrial carcinoma in literature and with best of our knowledge, no such case has been reported from India.

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