Indian Journal of Pathology and Oncology 2023;10(1):98–102

Content available at: https://www.ipinnovative.com/open-access-journals

Indian Journal of Pathology and Oncology

Journal homepage: www.ijpo.co.in

Case Report

Adult granulosa cell tumor of ovary in a young female: A rare case report

Sakshi Sumedh Agrawal[1], Nandkumar V Dravid[1], Sumedh S Agrawal[2], Anand Tambat[3], Priyanka Uttam Patil[1,*]

[1]*Dept. of Pathology, ACPM Medical College, Dhule, Maharashtra, India*
[2]*Dept. of Medicine, Shri Bhausaheb Hire Government Medical College, Dhule, Maharashtra, India*
[3]*Dept. of Gynaecology, JMF's ACPM Medical College & Hospital, Maharashtra, India*

ARTICLE INFO

Article history:
Received 09-12-2022
Accepted 15-01-2023
Available online 16-03-2023

Keywords:
Ovary
Granulosa cell tumour
Sex cord stromal tumors

ABSTRACT

Granulosa cell tumours (GCT) belong to the group of sex cord and stromal tumours of ovary. Adult granulosa cell tumours account for approximately 1% of all ovarian tumours and 95% of all granulosa cell tumours. They are found more often in postmenopausal than premenopausal women, with a peak incidence between 50 and 55 years of age. We present the case of a 35-year female who came with white discharge, irregular menses and excessive bleeding during menses since 5 to 6 months. The complete blood picture with peripheral smear examination, kidney and liver function tests were all within normal limits. CT abdomen was advised which revealed a large solid cystic lesion of left ovarian origin. Surgical intervention was done and histopathology revealed adult granulosa cell tumor of ovary.

1. Introduction

Solid ovarian tumours comprises a small percentage of ovarian tumours, that too less common in young women. Dysgerminoma is the commonest ovarian tumor in younger age groups. Diagnosis of solid tumor in young female is often delayed because they mimic common conditions like pedunculated fibroids, fibromas, thecomas, polycystic ovary, malignant ovarian tumors, or an ovarian torsion.[1]

We present a rare case of granulosa cell tumor of ovary in a young female.

2. Case Report

A 35-year old multiparous female presented in the gynecology out patient department with the chief complaints of white discharge, irregular menses and excessive bleeding during menses since the past 5 to 6 months. She was married since 17 years and had four uneventful childbirths. She had 60-90 days menstrual cycle with a flow of 15-16 days.

There was no history of anorexia or weight loss, urinary symptoms, postcoital bleeding or dyspareunia. She did not use any hormonal contraceptives or ovulation-inducing drugs. There was no family history of a similar illness. She was non diabetic, non hypertensive, non smoker and non alcoholic.

On general examination the patient was moderately built and pale, rest all vitals being within normal limits. Cardiovascular and respiratory examination did not reveal any abnormality.

However she had uniformly distended abdomen with no other scars or irregularities. Speculum examination showed a bulky healthy-looking cervix and the cervical os was patulous on digital examination. On bimanual examination uterus could not be palpated separately due to per abdomen mass.

* *Corresponding author*.
E-mail address: piupatil2695@gmail.com (P. U. Patil).

https://doi.org/10.18231/j.ijpo.2023.021

Complete blood count showed 11.7% hemoglobin and WBC count was 11800 cells/mm^3. Peripheral smear examination, renal and liver function tests and urine examination were all normal. A cervical pap smear was advised which was negative for any intra epithelial lesion or malignancy; however the smear was inflammatory and showed fungal colonies consistent with candida species.

CT scan of abdomen and pelvis was planned which showed a large solid cystic lesion measuring 19.2 x 11 x 8.4 cm present in midline and extending on left side. There was enhancement of solid component on CECT, left ovary was not seen separately from the lesion. Lesion was abutting the uterine fundus. Uterus appeared normal with endometrial thickness being 13mm. Right ovary was normal.

On admission tumor markers were done which had normal levels of CA-125, beta hCG and alpha feto protein. Chest radiography did not reveal any remarkable findings.

All these reports suggested a benign etiology of the mass. An initial diagnosis of benign left ovarian endometrioma or dermoid cyst was made. Total hysterectomy with left salpingo-oophorectomy was planned. Hemorrhagic peritoneal fluid was seen on opening the abdomen. Left ovarian mass of 20x10x10 cms was identified with intact capsule.

On receipt of the specimen in pathology department, uterus & cervix was unremarkable with left ovarian encapsulated mass measuring 21 × 15 × 8 cm and stretched out tube over it. Cut section of the lesion showed solid grey white to yellow tumor with tiny multiple cysts, few of which were filled with blood. No normal ovarian stroma was identified.

Histological examination revealed a tumor consisting of neoplastic granulosa cells which were monomorphic, with pale and scanty cytoplasm, few showing coffee bean nuclei organized diffusely and into trabeculae, compact clusters, microfollicles and macrofollicles. Few Call-Exner bodies and some mitotic figures were seen.

The tubal wall had normal structure without tumor invasion.

Additionally, endometrium showed hyperplasia without atypia and cervix was unremarkable.

Her post-operative period was uneventful, and she was discharged from the hospital on 13^{th} post-operative day.

On discharge, she was advised for a consultation with medical oncologist and also to continue her follow-up care with the gynecology team at our hospital.

3. Discussion

GCTs are derived from the granulosa cell layer of the ovarian follicles. Normally, these cells proliferate in response to rising circulating gonadotropins and decline in response to circulating testosterone. They normally produce estradiol, sex steroids and peptides necessary for ovulation. Excess estradiol, when sensed by the hypothalamus and anterior pituitary, decreases the production of gonadotropin-releasing hormone, FSH, and LH.[2,3]

Granulosa cell tumour (GCT) is extremely rare, sex cord stromal tumours constituting only 1% to 2% of all ovarian malignancies.[4] This is in accordance with the studies of Kanthikar et al,[5] Amita P et al[6] and Sharma et al[7] who in their studies on classification of ovarian tumours found the incidence of adult granulosa cell tumour between 1-2%. However, study done by Pilli G et al[8] and our present study found the incidence of adult granulosa cell tumour to be 3.54% and 3.7% respectively.

On the basis of age of onset and clinicopathological characteristics, these tumours are subdivided into two distinct forms, the adult type and the juvenile type representing 95% and 5% of the tumours, respectively.[4]

Most of the adult GCT present in postmenopausal women, with a peak incidence between 50 and 55 years.[2] However in our case, the patient was just 35 years of age.

Chromosomal abnormalities have been recently evaluated in granulosa cell tumors. These abnormalities include trisomy 12, monosomy 22, and deletion of chromosome 6. Peutz Jeghers syndrome and Potters syndrome show a syndromic association with GCT of ovary. In the present case, chromosomal studies were advised to the patient at discharge.

Continuous exposure to ovulation induction drugs like selective estrogen receptor modulators (SERM), clomiphene citrate, gonadotropins may also increase the risk of GCT.[9] However the patient denied any intake of ovulation induction drugs.

Clinical symptomatology is not specific for these tumors, but is most often manifested by an increase in abdominal volume with diffuse abdominal pelvic pain sometimes associated with cycle disorders, postmenopausal metrorrhagia and infertility. Their hyper-estrogenic character explains the appearance of endocrine manifestations and their association with other estrogen-dependent pathologies such as endometrial hyperplasia with or without atypia.[10] In this case also the patient presented with menstrual problems. And on histopathological examination the endometrium was found to be hyperplastic without any atypia.

The radiological findings of the GCT vary from solid mass to the cystic lesion and some may also present with hemorrhage. The two most common classifications are multiseparated cystic mass and unlobulated solid mass with cystic portions.[11] However none of these are diagnostic. In the present case, the radiological findings were suggestive of a large solid cystic lesion.

Similar to this case in majority of case reports the median tumor size was of 20 cm (4-33cm).[12]

Elevated levels of CA 125 is seen in 42% of cases (13/31) of GCT in a study conducted by Dridi et al.[12] However in our case the levels of CA 125 were within normal limits.

Table 1: Showing the incidence of adult granulosa cell tumor of ovary in different studies

WHO Classification of Ovarian Tumors	Pilli G et al[8] (2002) (n=282)	Kanthikar et al[5] (2014) (n=145)	Amita P et al[6] (2018) (n=162)	Sharma et al[7] (2020) (n=130)	Present Study(2022) (n=137)
Epithelial Tumors					
Serous	31.32%	36.36%	58.6%	50.77%	33.33%
Mucinous	19.5%	10.90%	18.6%	23.85%	40.74%
Endometriod Tumor	-	1.8%	-	-	-
Germ Cell Tumors					
Benign Cystic Teratoma	15.6%	10.90%	16.6%	16.92%	11.11%
Dysgerminoma	-	1.8%	1.3%	0.77%	-
Struma Ovarii	0.7%	1.8%	-	-	-
Sex Cord Stromal Tumors					
Granulosa Cell Tumor	3.54%	1.8%	0.6%	1.54%	3.7%
Fibroma	-	3.6%	3.1%	-	-
Metastatic Tumors					
Krukenberg	2.31%	3.6%	-	2.31%	-

Inhibin acts as a granulosa cell growth factor and its levels reflects the tumor burden so it can be used as a tumor marker. But as GCT is diagnosed in pathological specimen, serum inhibin is not done in preoperative period.[13] Similar to this case serum inhibin was not done in any case in a large retrospective study done by Dridi et al.[12] In our case also, serum inhibin was not done as there was no differential diagnosis of GCT pre-operatively.

GCT are usually diagnosed from the pathology specimen although a preoperative diagnosis can be suspected based on presence of an adnexal mass with features of hyperestrogenism, thickened endometrium and elevated serum inhibin.[13] However, in this present case there was no clinical features of hyperestrogenism.

The primary treatment consist of complete removal of tumor by adequate resection.[14] Surgical staging remains the initial management of a suspected case of GCT. The principles of surgery are similar to epithlial ovarian tumor. Nodal dissection is not a significant factor for survival and is not recommended in surgical staging of GCT.[9] In this case the tumour was resected completely, however the surgical staging could not be done.

On gross section, we found that the tumor was solid and cystic, the cysts were multilocular with a smooth internal surface filled with coagulated blood with ill-defined areas of hemorrhage, separated by solid tissue having variegated appearance with focal areas of necrosis and hemorrhage.

On microscopic examination, the architecture varied with the presence of microfollicular, trabecular, tubular, solid and diffuse pattern. Tumor consisted of small cells with a high nucleo-cytoplasmic ratio, few having coffee bean nuclei with a discrete nucleolus. All these findings are similar to the findings of Raivoherivony et al.[15] who reported similar findings in a case report of GCT of ovary.

Spread of granulosa cell tumors is local, by direct extension and intraperitoneal seeding. The tumors may also spread hematogenously, and patients can develop metastases in the lungs, liver, and brain years after initial diagnosis.[16] However in the present case the tumor was limited to ovary on presentation. And follow up needs to be done to know the further status of spread.

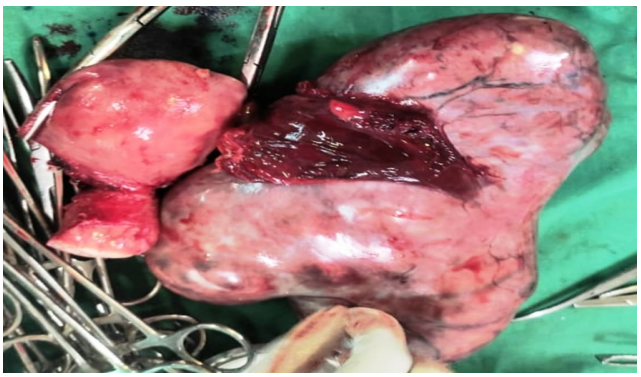

Fig. 1: Showing intra operative picture of Granulosa Cell Tumor

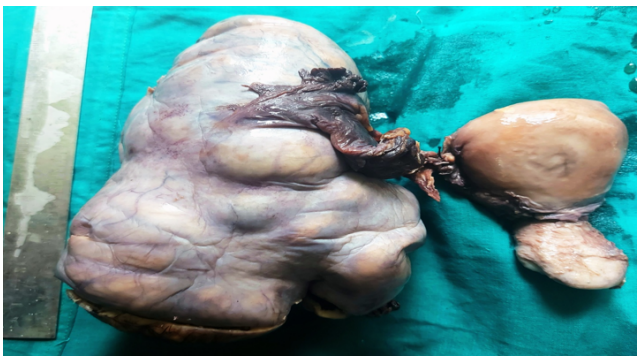

Fig. 2: Showing encapsulated smooth lobulated surface tan-yellow in colour

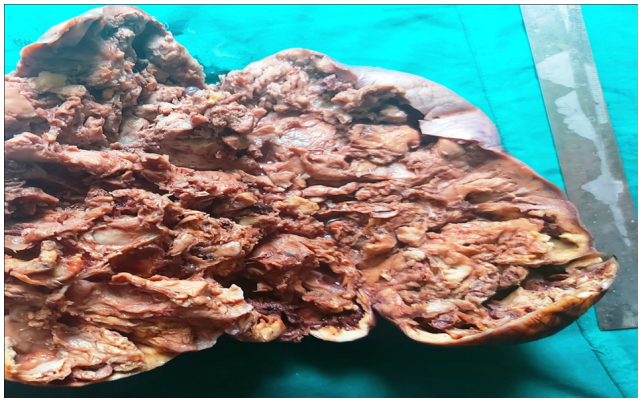

Fig. 3: Showing tan-yellow hemorrhagic cystic mass

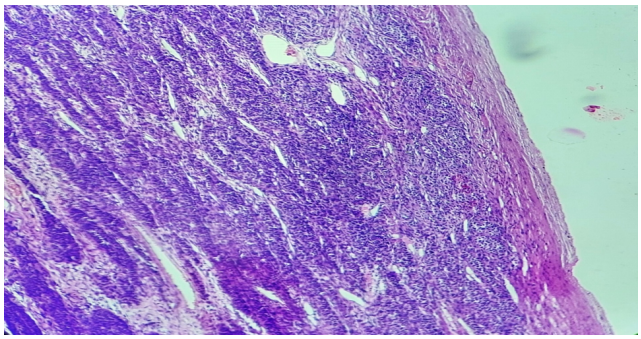

Fig. 4: Showing cystic areas lined by nests of tumor cells

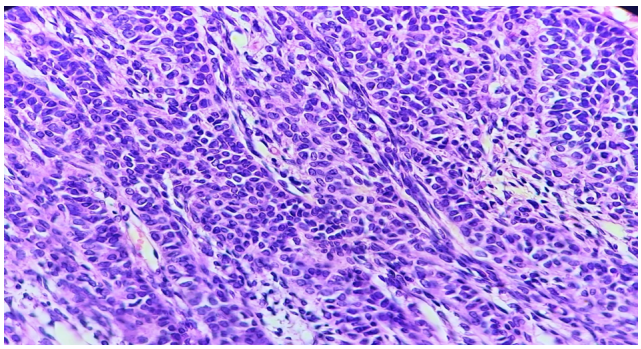

Fig. 5: Showing tumor cells having pale, uniform, round oval nuclei with irregular nuclear membranes

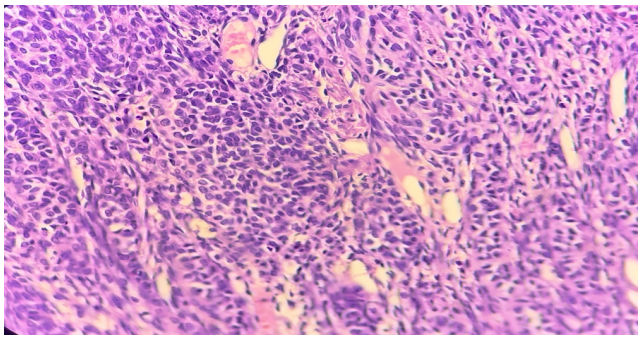

Fig. 6: Showing carl exner bodies

GCTs can cause endometrial cancer due to its feature of continuous and unopposed secretion of estrogen by the ovary; most of them are well-differentiated endometrioid adenocarcinomas that carry a good prognosis when detected early. Endometrial pathology in the form of hyperplasia is a common finding.[14] In the present case also, we found concomitant endometrial hyperplasia without atypia.

In the study by Dridi et al.[12] median survival of patients who underwent optimal cytoreduction was 60 months in contrast to 19 months for those who did not, in advanced cases. In the present case follow up needs to be done to know the survival outcomes of patient.

To summarise, whenever the patient presents with large, unilateral, solid, cystic, adnexal mass associated with abnormal bleeding per vaginum, differential diagnosis can be GCT, primary endometrial cancer metastasising to the ovary, primary ovarian cancer with metastasis to the uterus and synchronous epithelial ovarian and endometrial cancer.[17] In this case the endometrium showed only proliferative changes with no atypical / neoplastic cells.

4. Conclusion

Granulosa cell tumor of ovary is a rare ovarian entity. Complete workup with imaging and tumour markers can support the diagnosis. Estradiol secretion is the reason for symptoms and signs at presentation, which include vaginal bleeding , pelvic mass, pelvic pain or infertility. Tumor rupture may cause abdominal pain and hemoperitoneum. The initial treatment of choice is surgery, which is necessary for histological diagnosis, appropriate staging, and debulking. Serum inhibin test as a tumor marker of granulosa cell tumor is usually run in retrospect after histopathological report. An endometrial assessment should be done once the diagnosis of granulosa cell tumors is confirmed. Though granulosa cell tumour is a tumour with low malignant potential, but it has a high chance of recurrence even years after apparent clinical cure of the primary tumor. So lifelong follow up with clinical examination and tumor markers like inhibin B is recommended. Other than stage of the disease, the other prognostic factors like age, tumor size, rupture of tumor, mitotic activity are not able to predict recurrences accurately. Adequate counseling followed by long-time follow-up with specialists in the multidisciplinary team is recommended to ensure thorough recovery and proper care. In patients with desire for fertility, a fertility preserving surgery with endometrial biopsy is safe and chemotherapy may be used if indicated without adversely affecting the chance and outcome of future pregnancies.

5. Source of Funding

None.

6. Conflict of Interest

None.

References

1. Paul PG, Thakur S, Annal A, Paul G, Chowdary KA. Incidental diagnosis of granulosa cell tumour in a 25-year-old woman. *Int J Reprod Contracept Obstet Gynecol*. 2021;10:1202–4.
2. Kim YS, Lee JH. A case report of ovarian granulosa cell tumor in patient with polycystic ovarian syndrome. *Medicine (Baltimore)*. 2021;100(50):e28261.
3. Joshi R, Baral G, Malla K. Ovarian Adult Granulosa Cell Tumor - a rare case report. *Nepal J Obstet Gynaecol*. 2018;13(1):57–60.
4. Bajpai D, Shanmugham D, Radhakrishnan V. Adult granulosa cell tumor presenting as massive ascites as the only sign-a case report. *Int J Med Rev Case Rep*. 2022;6(1):98–100.
5. Kanthikar SN, Dravid NV, Deore PN, Newadkar DB, Suryawanshi KH. Clinico-histopathological analysis of neoplastic and non-neoplastic lesions of the ovary: a 3-year prospective study in dhule, north maharashtra, India. *J Clin Diagn Res*. 2014;8(8):4–7.
6. Patel AS, Patel JM, Shah KJ. Ovarian tumors - Incidence and histopathological spectrum in tertiary care center. *Valsad IAIM*. 2018;5(2):84–93.
7. Sharma P, Rao PS, Mogra N, Talreja K. Histopathological study of ovarian tumours in a tertiary healthcare centre of southern Rajasthan. *Indian J Pathol Oncol*. 2020;7(4):561–6.
8. Pilli G, Sunita KP, Dhaded AV. Ovarian tumours: A study of 282 cases. *JIMA*. 2002;100(7):1–6.
9. Azariah MB. Granulosa Cell Tumors of Ovary - A Systematic Review. *Sch J Med Case Rep*. 2009;(7):690–5.
10. Moustaide H, Taheri H, Benkirane S, Saadi H, Mimouni A. Ovarian Adult Granulosa Cell Tumor: Report of 3 Cases. *J Clin Case Rep*. 2017;7:1062. doi:10.4172/2165-7920.10001062.
11. Chen. A late recurring and easily forgotten tumor: ovarian granulosa cell tumor. *World J Surg Oncol*. 2012;85. doi:10.1186/1477-7819-10-85.
12. Dridi M, Chraiet N, Batti R, Ayadi M, Mokrani A, Meddeb K, et al. Granulosa Cell Tumor of the Ovary: A Retrospective Study of 31 Cases and a Review of the Literature. *Int J Surg Oncol*. 2018;2018:4547892. doi:10.1155/2018/4547892.
13. Kottarathil VD, Antony MA, Nair IR, Pavithran K. Recent advances in granulosa cell tumor ovary: a review. *Indian J Surg Oncol*. 2013;4(1):37–47.
14. Kolli SN, Agrawal M, Khithani Y, Kotdawala K. A rare case of adult granulosa cell tumor of ovary as a cause of huge abdominal mass and postmenopausal bleeding. *J Datta Meghe Inst Med Sci Univ*. 2020;15(4):675–8.
15. Raivoherivony ZI, Rakotondrainibe FN. Adult Granulosa Cell Tumor in a Young Woman: A Case Report and Literature Review. *Open J Pathol*. 2020;10:124–8.
16. Koukourakis GV, Kouloulias VE, Koukourakis MJ, Zacharias GA, Papadimitriou C, Mystakidou K, et al. Granulosa Cell Tumor of the Ovary: Tumor Review. *Integr Cancer Ther*. 2008;7(3):204–15.
17. Medha PB, Dave P, Parekh C. Case Report on Synchronous Adult Granulosa Cell Tumour and Endometrial Cancer. *Gujarat Cancer Soc Res J*. 2020;22(1):21–2.

Author biography

Sakshi Sumedh Agrawal, Senior Resident https://orcid.org/0000-0002-0958-1281

Nandkumar V Dravid, Professor and Head

Sumedh S Agrawal, Assistant Professor

Anand Tambat, Professor

Priyanka Uttam Patil, Junior Resident

Cite this article: Agrawal SS, Dravid NV, Agrawal SS, Tambat A, Patil PU. Adult granulosa cell tumor of ovary in a young female: A rare case report. *Indian J Pathol Oncol* 2023;10(1):98-102.