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ADULT GRANULOSA CELL TUMOUR - A CASE REPORT OF A RARE ENTITY

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ABSTRACT Adult granulosa cell tumour is rare ovarian malignancy and constitutes 12% of sex cord stromal tumours and 1-2% of all ovarian malignancies. Adult GCT's peaks it's incidence in women at 50-55 years of age. In this case report a rare case of adult granulosa cell tumour is described. 60years old woman, P5L5 previous vaginal delivery, attained menopause 10 years had complaints of postmenopausal bleeding and abdominal pain for past 10 days. On examination per abdomen soft, not tenderness, no mass felt and no evidence of ascites. On per vaginal examination uterus anteverted, normal size , no cervical motion tenderness, in right fornix tense non tender swelling of 8*7 cm with restricted mobility and variable consistency was felt, no tenderness or mass appreciated in left fornix. USG and CECT PELVIS showed 7 x7.8 x 9.9 cm Right adnexal mass with variable consistency, irregular margins abutting the appendix and right ureter. Right ovary not separately visualized. Left ovary and uterus normal. Proceeded with staging laparotomy, right ovarian cystectomy done and sent for frozen section showed Granulosa cell tumour and then we proceeded with Total abdominal hysterectomy with bilateral salpingoopherectomy, infracolic omentectomy and right side pelvic nodal dissection. Patient was asked to followup with INHIBIN B after next 3 months. Though the granulosa cell tumour is a rare entity, it has good prognosis. Early suspicion, early diagnosis, appropriate management, histopathology and followup plays a key role in better management and increased survival rates.

KEYWORDS : Granulosa cell tumour, sexcord stromal tumours, postmenopausal bleeding, CECT pelvis, INHIBIN B.

INTRODUCTION

Adult granulosa cell tumours (GCT) consists of 1-2% of all ovarian tumors and 12% of all sex cord stromal tumors [1-3] .Granulosa cell tumours (GCT) are estrogen secreting tumors that can be seen in women of all ages . They are classified as Adult and Juvenile types . Incidence of GCT is 5 % in prepubertal girls and 95% in reproductive and postmenopausal years[4,5,6,7] . Bilateral occurence in only 2% of patients. 75% are associated with sexual pseudoprecocity because of the estrogen secretion [5] .

Case Report -

60 years old, Mrs. XX , obstetric score P5L5, previous 5 vaginal births, sterilised, attained menopause 10 years back , came with complaint of postmenopausal bleeding Pervaginum and abdominal pain for 10days. She changed 2 pads/day and not associated with clots. No complaint of acute abdomen or vomitings.

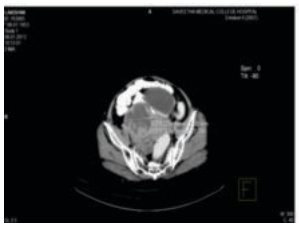
She attained menarche at 13 years and had had regular menstrual cycles. Married since 45 years, non consanguineous marriage . She had 5 term normal vaginal deliveries, LCB 25 years . No significant past , family or drug history. History of Thyroidectomy 5 years ago. On GENERAL EXAMINATION vitals stable, thyroidectomy scar seen , Breast examination done- normal. PER ABDOMEN - Sterilization scar present. On palpation- no tenderness, mass, rigidity or guarding or evidence of free fluid. PER SPECULUM- cervix healthy, bleeding through so present.

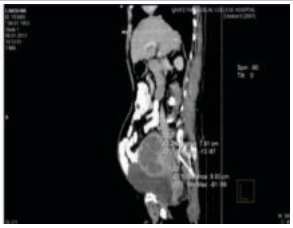
PER VAGINUM- uterus anteverted, normal size, mid position, no cervical motion tenderness, in right fornix a tense non tender swelling of 8*7 cm with restricted mobility and variable consistency was felt, no tenderness or mass appreciated in left fornix. Complete blood count, Liver function tests, Renal function tests, Thyroid function tests, ECG, Chest X RAY are within normal limits. CA 125 noted to be 13.67 IU/ml. Pap smear: negative for intra epithelial lesion . USG :Complex Right ovarian multiloculated cystic lesion likely malignant of size 8*7.8 cm noted. Uterus and left ovary normally visualized,ET 9 mm . Risk Of Malignancy Index (RMI) calculated RMI = U X M X S X Ca125 (U= ultrasound score , M= menopausal score , S= size of tumor) [Yanamoto et al. European journal of Obstet Gynaecol Reprod Biol.2009] . RMI = 4*4*42*13.67 = 433.44 . RMI <450 shows clinically a low malignant potential functioning ovarian tumour. CECT PELVIS :good contrast excretion , 7 x7.8 x 9.9 cm Right adnexal mass with variable consistency, irregular margins abutting the appendix and right ureter .Right ovary not separately visualized. Left ovary and uterus normally visualized .

Endometrial thickness 9 mm . No retroperitoneal lymph nodes or abdominal implants. No superficial or deep liver metastasis. Cervical biopsy revealed chronic nonspecific cervicitis with squamous metaplasia. Endometrial sampling revealed proliferation phase endometrium and no evidence of hyperplasia or malignancy. Anesthesia fitness was obtained and patient underwent Staging laparotomy . Intra op - no ascites, peritoneal washings sent for cytology. 10*10 cms tumor was identified arising from right ovary, no capsular rupture and no tumour on surface of ovary.

Uterus atrophic. Left tube and ovary were normal. Right ovarian cystectomy done and send for frozen section . Frozen section findings - Adult granulosa cell tumours. Proceeded with Total abdominal hysterectomy , bilateral salpingoopherectomy and infracolic omentectomy and right side iliac lymphnode dissection done and sent for HPE. Tumor surgically staged as STAGE 1A after palpation of upper abdomen and liver under surface.

HPE FINDINGS- ADULT GRANULOSA CELL TUMOR.Granulosa cells form rosettes around a eosinophilic material - call exner bodies. Scanty cytoplasm with oval angular grooved nuclei- coffee bean nucleus. Patient was advised to followup with INHIBIN B after 3 months.

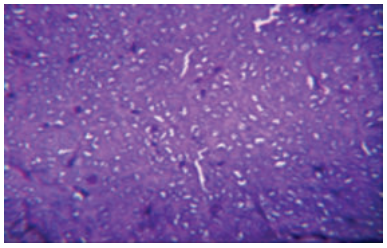




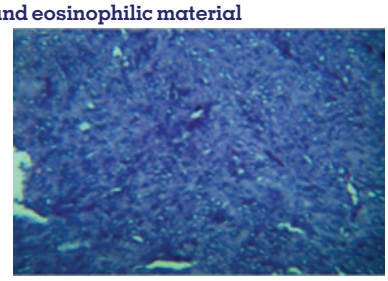
A) AXIAL CT SECTION **B) PARASAGITAL CT SECTION**

7*7.8*9.9 cm malignant right ovarian tumour with no lymph nodes and no metastasis.

Histopathology Imagings



C) CALL EXNER BODIES- Rosette formation by granulosa cells around eosinophilic material



D) COFFEE BEAN NUCLEUS- scanty cytoplasm with oval angular grooved nuclei

DISCUSSION-

Granulosa cell tumor of ovary was described by Rokintansky in 1855 [8,9]. Occurrence of GCT's are rare and these malignant tumors are clinicopathologically differentiated into adult and juvenile type. Adult type is most common among GCT's and occurs in perimenopausal and post menopausal age group with peak incidence at 50-55 years. In almost 98% of the patients it has unilateral occurence. Most of the patients in reproductive age group shows menstrual irregularities and secondary amenorrhea and most of the post menopausal women present with abnormal uterine bleeding[4,5,6,10,11] .

As GCT's are estrogen secreting tumors , 75% of patients in prepubertal age presents with sexual pseudo precocity[5]. In 5% of cases , endometrial cancer occurs in association with GCT and 25–50% are associated with endometrial hyperplasia [4,5,6,10,11]. Ascites might be present in 10% of cases and patients may rarely have pleural effusion [4,5]. Most commonly GCT's are hemorrhagic but rarely they rupture. [Adult type granulosa cell tumours of ovary has somatic missense point mutation in the gene encoding the forkhead box protein L2 FOXL2] .[FOXL2 402 CG leads to a gain or change of function and is believed to be a driver mutation for adult granulosa cell tumors] [12,13]. Most of the granulosa cell tumors are diagnosed at stage I and recurrence rate after diagnosis is 5-30% [14]. Metastasis can occur to lungs, liver, and brain and most commonly occurs by hematogenous spread [7,15]. Granulosa cell tumors secrete INHIBIN and it is important marker for diagnosis and prognosis [16-20]. Inhibin B is more predominant than Inhibin A and acts as a better marker for followup of granulosa cell tumors [19,21]. [Antimüllerian hormone (AMH) or Müllerian inhibitory substance (MIS), is produced by granulosa cells, and is emerging as a potential marker for these tumors (20)]. As granulosa cell tumors are unilateral in 98% of the cases and most of the cases are diagnosed at stage IA, unilateral salpingo oopherectomy remains as appropriate therapy [22]. In premenopausal women endometrial curettage sampling plays a key role due to associated risk of adenocarcinoma of endometrium [4]. Few retrospective studies shows postoperative chemotherapy with BEP, EP, PAC, carboplatin and paclitaxel prolongs progression free interval in women with stage III and IV. Adjuvant radiotherapy doesn't play any role in GCT's. The median time to relapse is approximately 4 to 6 years after initial diagnosis [14,22,23,25].

In adult tumors, cellular atypia, mitotic rate, and the absence of Call-Exner bodies are the only significant pathologic predictors of early recurrence [24]. 10 year survival rates are 87.2%,75%,20%,0% for stage 1,2,3,4 respectively[3,26,27]. The presence of residual disease was found to be the most important predictor of progression-free survival, but DNA ploidy was an independent prognostic factor.

CONCLUSION-

Adult Granulosa cell tumour is a rare entity but early stages have a good prognosis. Early suspicion, early diagnosis, appropriate management, histopathology and followup plays a key role in better management and increased survival rates.

REFERENCES

1. Ukah CO, Ikpeze OC, Eleje GU, Eke AC. Adult granulosa cell tumor associated with endometrial carcinoma: A case report. J Med Case Rep 2011;5:340.
2. Adhikari RC, Jha A, Shayami G. Granulosa cell tumor of the ovary: A clinicopathological study of six cases. J Pathol Nepal 2011;1:96-9.
3. Sekkate S, Kairouani M, Serji B, Tazi A, Mrabti H, Boutayeb S, et al. Ovarian granulosa cell tumors: A retrospective study of 27 cases and a review of the literature. World J Surg Oncol 2013;11:142.
4. Segal R, DePetrillo AD, Thomas G. Clinical review of adult granu- losa cell tumors of the ovary. Gynecol Oncol. 1995;56:338–344.
5. Cronje HS, Niemand I, Barn, RH, et al. Review of the granulosa– theca cell tumors from the Emil Novak ovarian tumor registry. Am J Obstet Gynecol. 1999;180:323–328.
6. Aboud E. A review of granulosa cell tumours and thecomas of the ovary. Arch Gynecol Obstet. 1997;259:161–165.
7. Young R, Clement PB, Scully RE. The ovary. In: Sternberg SS, ed. Diagnostic Surgical Pathology. New York, NY: Raven Press, 1989: 1687.
8. Lee IH, Choi CH, Hong DG, Song JY, Kim YJ, Kim KT, et al. Clinicopathologic characteristics of granulosa cell tumors of the ovary: A multicenter retrospective study. J Gynecol Oncol 2011;22:188-95.
9. Rokitansky CV. Uberabnormalitiaten des corpus luteum. Allg Wien Med Z 1859;4:253-8.
10. Scully RE, Young RH, Clement RB. Tumors of the ovary, malde- veloped gonads, fallopian tube, and broad ligament. In: Atlas of Tumor Pathology: 3rd series, Fascicle 23. Washington, DC: Armed Forces Institute of Pathology; 1998:169–498.
11. Boyce EA, Costaggini I, Vitonis A, et al. The epidemiology of ovarian granulosa cell tumors: A case-control study. Gynecol Oncol. 2009; 115: 221–225.
12. Zhao C, Vinh TN, McManus K, et al. Identification of the most sensitive and robust immunohistochemical markers in different cat- egories of ovarian sex cord-stromal tumors. Am J Surg Pathol. 2009; 33:354–366.
13. Köbel M, Gilks CB, Huntsman DG. Adult-type granulosa celltumors and FOXL2 mutation. Cancer Res. 2009;69:9160–9162.
14. Malmström H, Högberg T, Risberg B, et al. Granulosa cell tumors of the ovary: Prognostic factors and outcome. Gynecol Oncol. 1994; 52:50–55.
15. Chechia A, Attia L, Temime RB, et al. Incidence, clinical analysis, and management of ovarian fibromas and fibrothecomas. Am J Obstet Gynecol. 2008;199:473.e1–e4.
16. Lappohn RE, Burger HG, Bouma J, et al. Inhibin as a marker for granulosa-cell tumors. N Engl J Med. 1989;321:790–793.
17. Hildebrandt RH, Rouse RV, Longacre TA. Value of inhibin in the identification of granulosa cell tumors of the ovary. Hum Pathol. 1997;28:1387–1395.
18. Richi M, Howard LN, Bratthauae GL, et al. Use of monoclonal antibody against human inhibin as a marker for sex-cord-stromal tumors of the ovary. Am J Surg Pathol. 1997;21:583–589.
19. Mom CH, Engelen MJ, Willemse PH, et al. Granulosa cell tumors of the ovary: The clinical value of serum inhibin A and B levels in a large single center cohort. Gynecol Oncol. 2007;105: 365–372.
20. Matias-Guiu X, Pons C, Prat J. Müllerian inhibiting substance, alpha-inhibin, and CD99 expression in sex cord-stromal tumors and endometrioid ovarian carcinomas resembling sex cord-stromal tumors. Hum Pathol. 1998; 29:840–845.
21. Chang HL, Pahlavan N, Halpern EF, et al. Serum Müllerian Inhib- iting Substance/anti-Müllerian hormone levels in patients with adult granulosa cell tumors directly correlate with aggregate tumor mass as determined by pathology or radiology. Gynecol Oncol. 2009;114: 57–60
22. Miller BE, Barron BA, Wan JY, et al. Prognostic factors in adult granulosa cell tumor of the ovary. Cancer. 1997;79:1951–1955.
23. Brown J, Sood AK, Deavers MT, et al. Patterns of metastasis in sex cord-stromal

tumors of the ovary: Can routine staging lymphadenec- tomy be omitted? Gynecol Oncol. 2009;113:86–90.
24. Zambetti M, Escobedo A, Pilotti S, et al. Cis-platinum/vinblastine/ bleomycin combination chemotherapy in advanced or recurrent granulosa cell tumors of the ovary. Gynecol Oncol. 1990;36:317–320.
25. Lauszus FF, Petersen, AC, Greisen J, et al. Granulosa cell tumor of the ovary: A population-based study of 37 women with stage I disease. Gynecol Oncol. 2001;81:456–460.
26. Stenwig JT, Hazekamp JT, Beecham JB. Granulosa cell tumors of the ovary. A clinicopathological study of 118 cases with long-term follow-up. Gynecol Oncol 1979;7:136-52.
27. Sehouli J, Drescher FS, Mustea A, Elling D, Friedmann W, Kuhn W, et al. Granulosa cell tumor of the ovary: 10 years follow-up data of 65 patients. Anticancer Res 2004;24:1223-9.