



## ADULT GRANULOSA CELL TUMOR OF OVARY – A DIAGNOSTIC CHALLENGE ON FROZEN SECTION.

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**ABSTRACT** **Background:** Adult granulosa cell tumor (AGCT) is the most common sex cord stromal tumor accounting for 1% of all ovarian neoplasms. Frozen section plays a vital role in the intraoperative diagnosis of ovarian neoplasms with 87.89% accuracy. We are presenting a case of AGCT which could not be diagnosed on frozen section due to absence of classical features. **Case Report:** A 42y/F presented with complaints of menorrhagia since 3 months. Ultrasonography was s/o ovarian mass. Ovarian tumor markers were within normal limit. Ovarian mass with intact capsule was received for frozen section, C/S-yellowish, solid-cystic. On frozen section sheets & trabeculae composed of polygonal tumor cells having vesicular nuclei, scant cytoplasm with ample mitosis were noted s/o malignant ovarian tumor. However, tumor type was not ascertained. HPE on extensive sampling showed focal areas with classical AGCT morphology. IHC findings confirmed the diagnosis of GCT. **Discussion:** Though frozen section has high diagnostic accuracy for ovarian tumors in borderline surface epithelial tumors and granulosa cell tumor making absolute diagnosis is difficult. AGCT with a diffuse pattern can be mistaken for poorly differentiated carcinomas, undifferentiated carcinomas, adenocarcinomas, and carcinoids all of which show morphological resemblance. It is crucial to accurately diagnose these tumors because of strikingly different prognosis. However, when classical cytological and architectural features of AGCT like grooved nuclei, diffuse pattern, Call Exner bodies are not seen, the diagnosis on frozen section becomes challenging. Presence of plenty mitotic figures makes this diagnosis even more difficult as was in our case. Scrape cytology may aid in diagnosis.

**KEYWORDS :** Frozen section; Adult Granulosa cell tumor; intra-operative; scrape smear cytology.

### INTRODUCTION

Adult granulosa cell tumor (AGCT) is the most common low grade indolent sex cord stromal tumor accounting for about 1% of all ovarian neoplasms. Frozen section plays a vital role in the intraoperative diagnosis of ovarian neoplasms with 87.89% accuracy (1,2). Ovarian neoplasms are categorized as surface epithelial tumors, germ cell tumors, sex cord stromal tumors and secondary malignancies,

The surgical options for benign, borderline, and malignant ovarian surface epithelial tumors vary. When a case is malignant, staging laparotomy is carried out, which entails bilateral salpingo-oophorectomy, pelvic and para-aortic lymph node biopsy (up to the level of the renal vein), omentectomy, multiple peritoneal biopsies and peritoneal cytology as well as total abdominal hysterectomy while for benign tumors, young women who wish to maintain their fertility are typically treated with a cystectomy, which involves removing the entire ovarian cyst or mass. However for borderline tumors, a cautious approach is typically taken, involving little omental sampling and skipping lymph node dissection, if the tumor is not clinically enlarged. Young patients can also choose fertility sparing measures. Even though there are several surgical therapeutic strategies for various tumor classifications, preoperative diagnosis is not always achievable, particularly for tumor markers. When fertility preservation is needed, especially in young females, intraoperative frozen sections become essential for directing surgical care. (3,4,5)

The use of frozen sections and cytological smears for intraoperative identification of ovarian pathology has been studied over the last few years. The majority of studies contrast the accuracy and efficacy of these two approaches. It has been demonstrated that cytological smears are a low-cost, simple method that can maintain cellular features. The diagnosis of some types of ovarian neoplasms can also be made more accurately and sensitively using frozen sections than with cytological smears alone. However, cytological smears should primarily serve as a very helpful complementary tool in frozen section diagnosis (6,7,8). We are presenting a case of Adult Granulosa Cell Tumour which could not be diagnosed on frozen section due to absence of classical features.

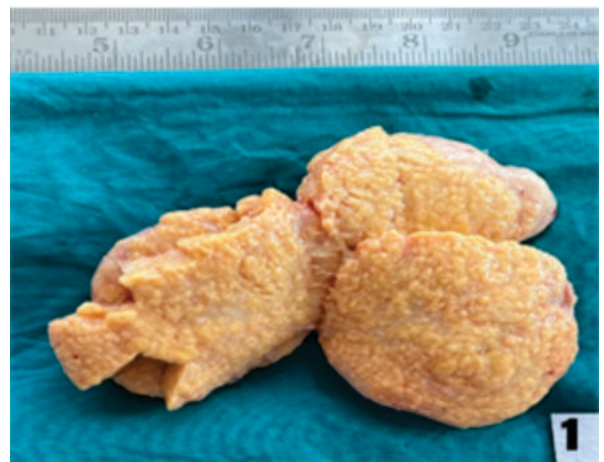
### Clinical Profile

A 42 years old female presented with complaints of menorrhagia since 3 months. On radiological investigations – hypoechoic mass lesion

with minimal internal vascularity is noted in right adnexa, s/o ovarian mass. Tumour markers, CA123, AFP, CA19.9, CEA, Beta HCG, Serum LDH were within normal limits. Intraoperatively specimen of right oophorectomy was sent for frozen section.

### Gross

Received ovarian mass measuring 10x8.5x3 cms with intact capsule. C/S – Yellowish, solid with areas of haemorrhage. (Fig 1)



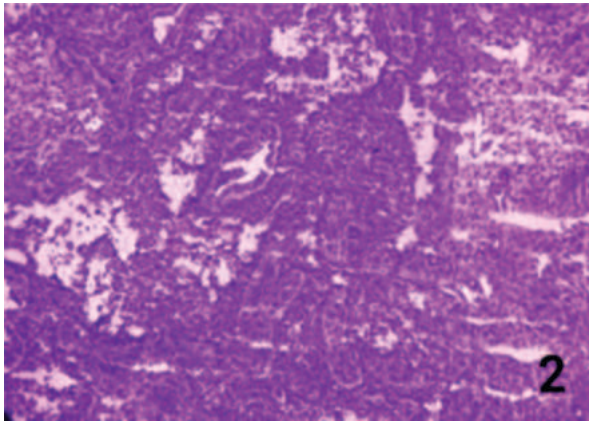
**Fig.1 – Ovarian Mass With Intact Capsule, C/s Shows Yellow, Solid Areas.**

### Histopathology

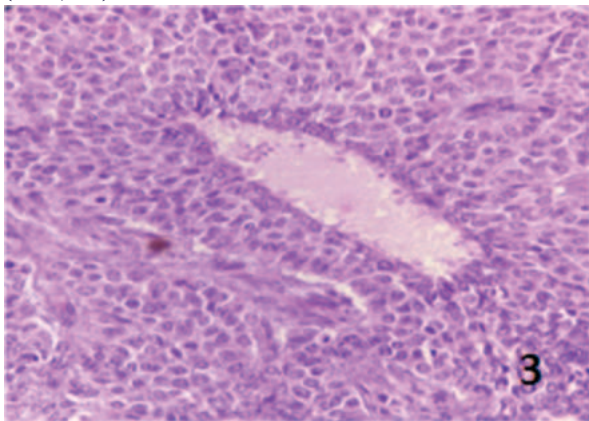
On frozen section, sheets & trabeculae composed of polygonal tumour cells having vesicular nuclei & scant cytoplasm with ample mitosis were noted. So the diagnosis was given as s/o malignant ovarian tumor. However, tumor type was not ascertained.

On routine histopathology, extensive sampling showed focal areas with classical granulosa cell tumor morphology with presence of call-exner bodies. On IHC, CD99 and Calretinin were found positive, while Inhibin A and Cytokeratin were focally positive. CAM 5.2 and GATA 3 were negative. Findings confirmed the diagnosis of Adult Granulosa

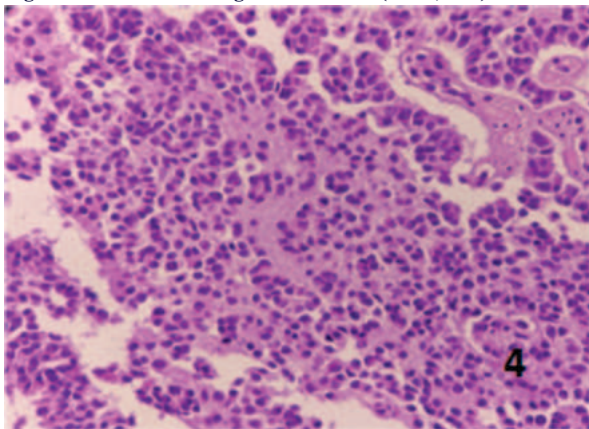
Cell Tumour.(Fig 2,3 &amp;4)



**Fig. 2 Tumour Cells Arranged In Sheets And Trabeculae (H&E,10X)**



**Fig.3 Tumor Cells Showing Macrofollicles (H&E, 20X)**



**Fig. 4 Tumor Cells Showing Occasional Call Exner Bodies (H&E, 20X)**

## DISCUSSION

Though, frozen section has high diagnostic accuracy for ovarian tumours, in borderline surface epithelial tumours and granulosa cell tumour making absolute diagnosis is difficult. AGCT with a diffuse pattern can be mistaken for poorly differentiated carcinomas, undifferentiated carcinomas, adenocarcinomas and carcinoids, all of which show morphological resemblance. It is crucial to accurately diagnose these tumours because of strikingly different prognosis. However, when classical cytological and architectural features of AGCT like grooved nuclei, diffuse pattern, Call Exner bodies are not seen, the diagnosis on frozen section becomes challenging. Presence of plenty of mitotic figures makes this diagnosis even more difficult as was in our case. Scrape cytology may aid in diagnosis (2,9,10).

Intraoperative frozen section could be misleading in the diagnostic evaluation of ovarian Granulosa Cell Tumors. In a study done by Di Cello A et al, out of 20 cases 12 cases were correctly identified at the

intraoperative frozen section as Granulosa Cell Tumors and 8 (32%) cases were misdiagnosed. This study concluded that frozen section appears to be an inadequate technique for the histopathological diagnosis of ovarian Granulosa Cell Tumors. (11)

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 (12).

Granulosa cell tumor of the ovary is a rare tumor. Imaging and tumor markers can support the diagnosis. Estradiol secretion causes symptoms like vaginal bleeding, pelvic mass, pelvic pain, or infertility. Tumor rupture may lead to abdominal pain and hemoperitoneum. Surgery is the initial treatment of choice for histological diagnosis, staging, and debulking. The serum inhibin test, a tumor marker for granulosa cell tumor, is usually done retrospectively after the histopathological report. In difficult cases high suspicion index and additional measures like scrape cytology might help. Once diagnosed, an endometrial assessment should be performed. Although granulosa cell tumors have low malignant potential, they have a high chance of recurrence even years after clinical cure. Lifelong follow-up with clinical examinations and tumor markers like inhibin B is recommended. (13,14,15,16)

In the present study, the major causes of diagnostic discrepancy were due to heterogeneous nature of the lesions (sampling error) and low-grade nuclear features (interpretive error).

## CONCLUSION

Frozen section still remains an important tool for diagnosis of ovarian tumours. The diagnostic errors during frozen section can be due to sampling error, misinterpretation or suboptimal slide preparation. These errors can be reduced by meticulous macroscopic examination, evaluation of multiple sections along with clinical and radiological findings. AGCT with a diffuse pattern can be mistaken for poorly differentiated carcinoma, endometrioid carcinoma and carcinoid tumor on frozen section. In such situations, the classical cytological and nuclear features might help in offering accurate diagnosis.

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