Section: Pathology

Original Research Article

GRANULOSA CELL TUMORS OF THE OVARY: A CLINICOPATHOLOGICAL STUDY FROM A TERTIARY CARE CENTER

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ABSTRACT

Background: Granulosa cell tumors (GCTs) are uncommon ovarian neoplasms comprising approximately 2% to 5% of all ovarian cancers and represent the most frequent malignant sex cord–stromal tumors. They are classified into adult (AGCT) and juvenile (JGCT) types and are characterized by diverse clinical presentations and histomorphologic patterns. This study describes the clinicopathological features of GCTs diagnosed at a tertiary care center. **Materials and Methods:** A retrospective descriptive study was conducted on patients who underwent surgery for ovarian lesions between July 2016 and July 2024 at Government Thoothukudi Medical College, Tamil Nadu. Histopathology records were reviewed to identify cases diagnosed as GCT. Clinical data, gross findings, microscopic features, mitotic index (per 10 high-power fields), capsular status and FIGO stage were analyzed. **Result:** Among 116 ovarian lesions operated during the study period, five (4.3%) were diagnosed as GCT post operatively. Four were AGCT and one was JGCT. The age ranged from 17 to 70 years (mean age for AGCT: 47 years). The common presenting symptoms were abdominal pain and abnormal vaginal bleeding. Tumor size ranged from 5 cm to 23 cm. Four patients were stage IA and one was stage IC2. All tumors were unilateral. Microscopically, AGCT cases demonstrated varied architectural patterns including microfollicular, trabecular, diffuse sheets and insular patterns. Call–Exner bodies and characteristic nuclear grooves were observed in all AGCT cases. The JGCT case lacked nuclear grooves and Call–Exner bodies and showed diffuse sheets with luteinized cells and mild to moderate atypia. Mitotic activity ranged from 1 to 22 per 10 high-power fields. Endometrial evaluation revealed proliferative endometrium in one, atypical hyperplasia in one and cystic glandular atrophy in one postmenopausal patient. **Conclusion:** GCTs are uncommon ovarian tumors that commonly present at an early stage. They exhibit variable histomorphology and the presence of nuclear grooves and Call–Exner bodies strongly supports the diagnosis of AGCT, although neither is pathognomonic. Complete surgical staging remains the cornerstone of management. Given the known potential for late recurrence, long-term follow-up is necessary.

INTRODUCTION

Granulosa cell tumors (GCTs) are rare ovarian neoplasms, accounting for approximately 2 % to 5% of all ovarian cancers.[1] They are the most common malignant sex-cord stromal tumors of the ovary. Based on clinicopathological features, GCTs are classified into adult (AGCT) and juvenile (JGCT) types. Approximately 95% of cases belong to the adult type. AGCT typically occurs in perimenopausal and early postmenopausal women, whereas JGCT is more common in children and young adults. These tumors are often hormonally active and may produce estrogen, leading to abnormal uterine bleeding and endometrial hyperplasia. Abnormal vaginal bleeding and abdominal pain are the common symptoms in GCT.[1-5]

Histologically, AGCT is characterized by diverse architectural patterns including microfollicular, trabecular, insular, macrofollicular and diffuse sheets. Call–Exner bodies and coffee-bean nuclei with longitudinal grooves are characteristic features. The FOXL2 mutation has been identified in approximately 95–97% of AGCTs and is considered a key molecular event in tumorigenesis.[6-9] JGCT lacks this mutation and demonstrates distinct histomorphological features.

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GCTs are generally prone for late recurrence, even decades after initial treatment. This study describes the clinicopathological characteristics of GCTs diagnosed at our institution over an eight-year period.

MATERIALS AND METHODS

This retrospective descriptive study included patients who underwent surgery for ovarian lesions between July 2016 and July 2024 at the Department of Surgical Oncology, Government Thoothukudi Medical College, Tamil Nadu. Out of 116 surgically treated ovarian lesions, five cases were diagnosed as granulosa cell tumor on postoperative histopathological examination. One patient operated for late recurrence of GCT was excluded to maintain homogeneity of primary cases. Clinical records were reviewed for demographic details, presenting symptoms and operative details. All available hematoxylin and eosin slides were retrieved and re-evaluated independently. Endometrial histology was evaluated in cases where hysterectomy was performed. Tumors were staged according to the FIGO staging system (2014 revision).

Microscopic parameters assessed included:

- Histological subtype (AGCT/JGCT)
- Architectural pattern
- Presence of Call–Exner bodies
- Nuclear grooves
- Degree of atypia
- Mitotic count (number per 10 high-power fields in most mitotically active areas)
- Capsular integrity
- Necrosis
- Adjacent organ involvement

Statistical Analysis: Data were entered into Microsoft Excel and analyzed descriptively. Continuous variables are presented as mean ± standard deviation (SD) and range. Categorical variables are expressed as frequencies and percentages. Given the small sample size, no formal inferential statistical testing was performed.

RESULTS

5 patients were diagnosed as GCT post operatively. Among the 5 patients, 4 were AGCT (80%) and 1 JGCT (20%). The age ranged from 17 to 70 years. The mean age of patients with AGCT was 47 years. The single JGCT case occurred in a 17-year-old patient. The overall mean age at diagnosis was 41.0 ± 19.6 years (range: 17–70 years).The common presenting symptoms were abdominal pain and abnormal vaginal bleeding. Preoperative imaging revealed complex adnexal masses with solid-cystic components in all patients.

Of those 5 patients, 3 underwent comprehensive staging laparotomy (60%) and 2 underwent fertility sparing staging laparotomy (40%). 4 were diagnosed at Stage IA and one at Stage IC2 (FIGO staging). All tumors were unilateral (right: 3 (60%); left: 2 (40%)). Tumor size ranged from 5 cm to 23 cm. Capsular breach was identified in 1 patient (20%). Grossly, all tumors exhibited solid-cystic morphology. Yellowish solid areas were consistently observed.

Histopathological Features [Table 1]

Among AGCT cases (n = 4):

- Call–Exner bodies: 4/4 (100%) [Figure 1]
- Nuclear grooves: 4/4 (100%) [Figure 2]
- Diffuse sheet pattern: 4/4 (100%)
- Microfollicular pattern: 3/4 (75%)

The JGCT case lacked Call–Exner bodies and nuclear grooves. Mitotic activity ranged from 1 to 22 per 10 high-power fields. The juvenile case showed tumor cells with abundant eosinophilic cytoplasm, some showing vacuolation with nuclei exhibiting mild to moderate pleomorphism [Figure 3]. No lymph node metastasis was identified in the staged cases. The endometrial study done in cases where hysterectomy was performed (3/5) showed proliferative phase in one patient (33.3%), atypical hyperplasia in one patient (33.3%) and cystic glandular atrophy in one post menopausal patient (33.3%).

Table 1: Histopathological features

Age, tumor type	Tumor size in cm	Cut surface	Capsule	Architectural patterns	Call – Exner bodies	Endometrium	FIGO stage
28 years AGCT	9x7	Multiloculated cyst filled with blood clot, Yellowish white solid areas present	Intact	microfollicular, trabecular, insular, diffuse sheets	Present	-	IA
42 years AGCT	5x5.5	Cyst with greyish yellow solid areas showing areas of hemorrhage	Intact	Diffuse Sheets	Present	Proliferative phase	IA
17 years JGCT	23x19x10	Multiloculated cysts with yellowish solid nodular areas	Intact	Diffuse Sheets, nodular aggregates, cells with leutinised cytoplasm, mild to moderate nuclear atypia	Absent	-	IA
48 years AGCT	16x11.5x5.5	Predominantly hemorrhagic with	Breach	Sheets, microfollicular, cords, nests	Present	Atypical Hyperplasia	IC2

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		focal grey white to yellowish areas					
70 years AGCT	16x15x8	Predominantly solid with numerous small cystic spaces and periphery showing focal yellowish firm areas with central hemorrhagic necrosis	Intact	Sheets, nest, trabecular, cords, Microfollicular, gyriform	Present	Cystic glandular atrophy	IA

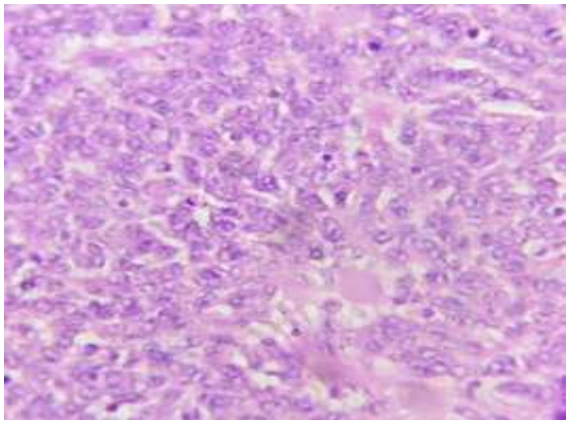

Figure 1: Call-Exner bodies

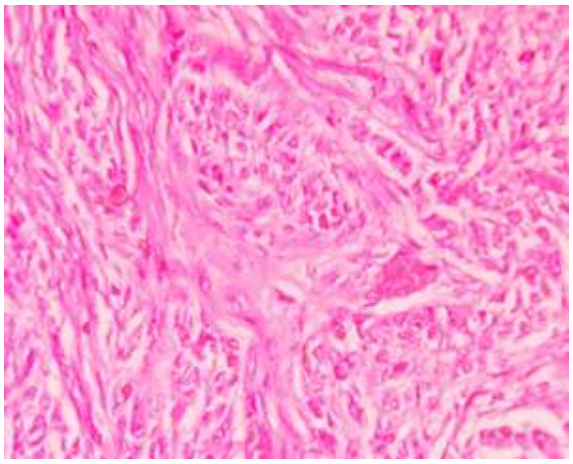

Figure 2: Tumor cells showing nuclear groove

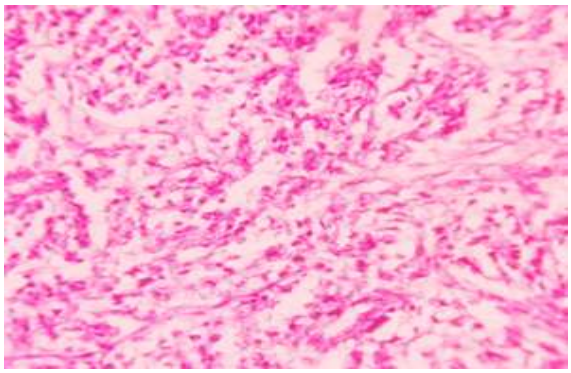

Figure 3: Juvenile Granulosa Cell Tumor

DISCUSSION

Granulosa cell tumors are uncommon ovarian neoplasms with a generally favorable prognosis when diagnosed at an early stage. In the present study, 80% of cases were diagnosed at stage IA, consistent with the literature reporting early-stage at presentation in most of the patients.[3-5] The mean age for AGCT (47 years) in our study aligns with previously published data.[1,3,5] The presence of abnormal uterine bleeding and associated endometrial pathology reflects estrogenic activity, a well-recognized feature of these tumors.

Stage remains as the most established prognostic factor in GCT.[1,3,10] In a study by Ranganath R et al., they found that sup-optimal cytoreduction, nuclear atypia and increased mitotic rate were associated with reduced overall survival.[2] In a study by Guleria P et al., disease recurrence was associated with higher stage.[3]

Histologically, AGCT demonstrated diverse architectural patterns, consistent with published series.[3] Although Call–Exner bodies are classically described, their absence does not exclude the diagnosis. Nuclear grooves are a characteristic and supportive finding in AGCT but are not pathognomonic, as they may be observed in other neoplasms. Molecularly, AGCT is strongly associated with FOXL2 mutation, which plays a significant role in tumorigenesis.[6-9]

The principal limitation of this study is the small sample size and retrospective design. Additionally, long-term follow-up data were not uniformly available, which is particularly relevant given the potential for late recurrence.

CONCLUSION

GCTs are rare ovarian neoplasms that frequently present at an early stage. They exhibit significant histomorphologic diversity. Nuclear grooves and Call–Exner bodies are characteristic and supportive features of AGCT but must be interpreted in the context of overall morphology. Complete surgical staging remains the cornerstone of management. Owing to the risk of late recurrence, prolonged surveillance is recommended.

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