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Case Series

Pathology Section

Clinicopathological Features of Adult Granulosa Cell Tumour of Ovary- A Case Series of 14 Cases

VARADHARAJAPERUMAL RADHAKRISHNAN[1], DHARMISHTHA NATVARLAL KAPADIYA[2], SIVA KALIYAMOORTHY[3], DEEPA SHANMUGAM[4], JAWAHAR RAMASAMY[5]

ABSTRACT

Adult Granulosa Cell Tumour (AGCT) is the most common sex cord stromal tumour of ovaries. These tumours in comparison with epithelial tumours are of low-grade malignant potential and have low recurrence rate after surgical procedure. In this case series, a retrospective search for ovarian AGCT cases from January 2016 till January 2021 was done. A total of 14 cases were included. Parameters studied in this case series were age, laterality, gross, architectural pattern, call Exner bodies, nuclear grooves, necrosis, mitotic count and tumour staging. After studying all the cases, it was reported that mean age of presentation was 44 years (range 21-64 years), unilateral with right-sided dominance (71.4%), grossly 78.5% of the cases were solid cystic with haemorrhagic area, with mean tumour size of 9 cm, 57.1% of the cases had call Exner bodies, and all the cases showed nuclear groves. Most of the cases, 85.7% presented with low mitotic count of <4/10 High Power Field (HPF). Rare presentation of endometroid carcinoma-endometrium World Health Organisation (WHO) Female Genital Tract (FGT) fifth edition), and mature teratoma of contralateral ovary were observed in one case each. This case series outlines characteristic histomorphological feature, frequent presentation at lower stage, and low mitotic count, these characteristic features act as prognostic marker for recurrence prediction.

Keywords: Ovarian, Pattern, Prognosis, Stage, Stromal tumour

INTRODUCTION

Ovarian Granulosa Cell Tumour (GCT) comes under group of sex cord stromal tumour and accounts for 1% of all ovarian tumour [1]. These tumours constitute two subgroups according to their clinical and histopathological features: Juvenile Granulosa Cell Tumours (JGCT) and AGCT [2]. AGCT is the most common sex cord stromal tumour of ovaries. It is frequently seen in perimenopausal age group and clinically present with abdominal symptoms or hyper estrogenic state such as uterine bleeding, endometrial hyperplasia and carcinoma [1]. These tumours in comparison with epithelial tumour were of low-grade malignant potential and have low recurrence rate after surgical procedure [3]. Surgery is the main line of treatment and lymphadenectomy should be avoided in early stage of presentation. Adjuvant therapy advised in advanced cases, high grade, tumour rupture [4]. The prognosis of the AGCT is generally good, overall survival and long-term survival reaching 75% and 90%. In Stage-I tumours, 5 years survival rate is between 92% to 100% [5].

A retrospective review of cases of ovarian AGCT was conducted from January 2016 to January 2021, after obtaining written permission from medical record department. The clinical details such as age, laterality, presenting complaints, surgical history and pathological findings including gross and microscopy of the lesions, were retrieved from Medical Record Department and distribution analysis was done.

CASE SERIES

During the period of six years from January 2016 to January 2021, 14 patients underwent surgery for AGCT of ovary. These 14 cases were included in this case series.

The mean age of patient was 44 years (Range 21-64), 64.2% of patients were <50 years. Most of the patients presented with post-menopausal bleeding (n=6, 42.8%) followed by abnormal uterine bleeding and abdominal pain in four cases each. One case presented with massive ascites. Ten cases (71.4%) involved the right-sided ovary. Nine cases (64.2%) underwent Total Abdominal Hysterectomy (TAH), and in five cases (35.8%) conservative surgery (salphingo-oophorectomy) was performed. Lymphnode dissection was performed in only two cases (14.3%), both the cases were free of tumour [Table/Fig-1,2].

S. No.	Age (years)	Presenting complaint	Tumour maximum diameter size (cm)	Ovary gross	Endometrium	Side	Procedure	Adult Granulosa Cell Tumour (AGCT) pattern
1.	42	Abdominal pain	4	Solid and cystic	Secretory	Right	TAH+BSO	cord, solid nest and insular patter
2.	37	Abnormal uterine bleeding	7	Solid and cystic	Not applicable	Right	Unilateral Ovariectomy	Microfollicular and diffuse
3.	40	Abnormal uterine bleeding	5	Solid and cystic	Proliferative	Left	TAH+BSO	Macro and microfollicular diffuse
4.	35	Abdominal pain	10	Solid and cystic	Not applicable	Right	Unilateral Ovariectomy	Microfollicular and diffuse
5.	38	Abnormal uterine bleeding	5.4	Solid	Proliferative	Right	TAH+BSO	Microfollicular, trabecular pattern
6.	51	Post-menopausal bleeding	8	Solid and cystic	Endometrial polyp	Right	TAH+BSO	Microfollicular, trabecular pattern

7.	37	Abnormal uterine bleeding	3.5	Solid and cystic	Not applicable	Left	Bilateral Ovariectomy. Right ovary - mature cystic teratoma	Solid, insular and macrofollicular
8.	44	Post-menopausal bleeding	6	Solid	Proliferative phase	Left	TAH+BSO	Water silk, insular, microfollicular
9.	64	Post-menopausal bleeding	8	Solid and cystic	Endometroid carcinoma- Uterine corpus Grade-1	Right	TAH+BSO+Bilateral salphingooophorectomy+Bilateral Pelvic lymphnode dissection	Insular, microfollicular, macrofollicular and trabecular
10.	51	Post-menopausal bleeding	9	Solid and cystic	Cystic atrophy	Right	TAH+BSO	Microfollicular and trabecular
11.	53	Post-menopausal bleeding	22	Solid and cystic	Proliferative phase	Right	TAH+BSO	Microfollicular and insular
12.	48	Abdominal pain	15	solid	Not applicable	left	Unilateral Ovariectomy	Gyriform sheet diffuse
13.	21	Abdominal pain	8	Solid and cystic	Not applicable	Right	Unilateral Ovariectomy	Microfollicular and diffuse
14.	54	Post-menopausal bleeding	11	Solid and cystic	Hyperplasia without atypia	Right	TAH+BSO+Bilateral salphingo-oophorectomy+Bilateral Pelvic lymphnode dissection	Solid, insular and macrofollicular

[Table/Fig-1]: Clinicopathological details.
Note: Total Abdominal Hysterectomy and Bilateral Salphingo-Oophorectomy (TAH-BSO)

S. No.	Clinical findings	Number (N=14) (%)
1.	**Age (years) (21-64)**	
	Mean age	44 years
	Pre menopause <50	9 (64.2)
	Post menopause >50	5 (35.8)
2.	**Clinical features**	
	Abdominal pain	4 (28.6)
	Postmenopausal bleeding	6 (42.8)
	Abnormal uterine bleeding	4 (28.6)
3.	**Laterality**	
	Left	4 (28.6)
	Right	10 (71.4)
4.	**Surgical procedure**	
	TAH+BSO*	9 (64.2)
	Conservative surgery	5 (35.8)
5.	**Lymphnode dissection**	
	Yes	2 (14.3)
	No	12 (85.7)
6.	**Tumour capsule rupture**	No

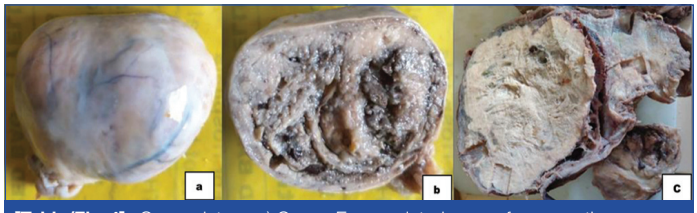
[Table/Fig-2]: Distribution of clinical findings (N=14)*.

Pathological Findings and Staging

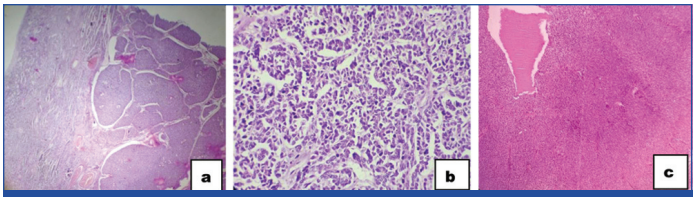
Of 14 cases, 78.5% cases showed solid cystic gross with haemorrhage areas. Mean Tumour diameter was of 9 cm (range 4-22 cm), No pre-operative or peri-operative tumour capsule rupture seen. Histopathological examination showed predominantly mixed architecture pattern such as solid, nesting, insular and trabecular patterns [Table/Fig-1-5]. Microscopically, eight cases (57.1%) showed call exner bodies and all the cases showed nuclear groove [Table/Fig-6]. Most of the cases (n=11, 78.6%) did not show any tumour necrosis. Twelve cases (85.7%) showed mitotic figure of <4/10 HPF. Along with AGCT, uterine corpus showed one case of each with Endometroid carcinoma- endometrium grade-1, and endometrial hyperplasia without atypia and in one other case along with AGCT, the contralateral ovary showed mature teratoma of ovary. Level of inhibin was assessed for follow-up and it was found elevated in 14 cases with mean value of 348 pg/ml and in one case CA 125 was elevated (>1000 U/mL) which was associated with massive ascites. International Federation of Gynecology and Obstetrics (FIGO) and American Joint Committee on Cancer (AJCC) prognostic staging was done for all 14 cases 92.8% (N=13) staged as FIGO IA, and one case of FIGO IIIC (elevated CA125, ascites case). Out of 14 cases only one case undergone adjuvant chemotherapy treatment and remaining 13 cases only follow-up was done as the stage was FIGO IA. Follow-up was done (ranging 11-84 months) by clinical examination and ultrasonography of pelvis and abdomen and serum inhibin levels every three months for the first two years and every six months till five years, no recurrence was noted [Table/Fig-3].

S. No.	Pathological findings	N (%)
1.	**Ovarian gross**	
	Solid	3 (21.3)
	Solid cystic	11 (78.5)
2.	**Tumour size (cm)**	
	Mean size	9 cm
3.	**Call exner bodies**	
	Yes	8 (57.1)
	No	6 (42.9)
4.	**Nuclear groves seen**	14 (100)
5.	**Necrosis**	
	Yes	3 (21.4)
	No	11 (78.6)
6.	**Mitotic figure (/10 HPF)**	
	Low mitotic count <4	12 (85.7)
	High mitotic count >4	2 (14.3)
7.	**Endometrial finding (N=9)** (Uterine corpus was not removed in 5 cases)	**N=9 (%)**
	No hyperplasia	07 (77.8)
	Hyperplasia	01 (11.1)
	Endometroid carcinoma- uterine corpus Grade-I	01 (11.1)
8.	**Mean serum Inhibin B level (N=14)**	348 pg/ml
9.	**FIGO Staging**	
	FIGO Stage-I A	13 (92.8%)
	FIGO Stage-III C	01 (7.2%)
10.	**Adjuvant therapy**	
	Chemotherapy given	01 (7.2%)

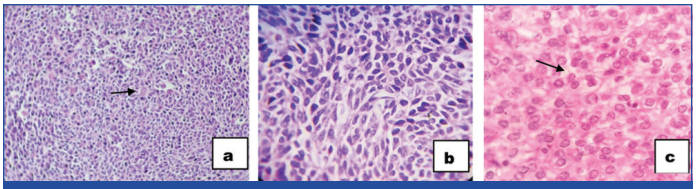
[Table/Fig-3]: Distribution of gross and histopathology findings.
FIGO: International federation of gynaecology and obstetrics



[Table/Fig-4]: Gross picture: a) Ovary- Encapsulated, no surface growth, no tumour capsule rupture; b) cut surface shows solid cystic and haemorrhagic; c) Circumscribed, solid, grey white homogenous cut surface.



[Table/Fig-5]: Showing various architecture: a) Circumscribed lesion with nodular (H&E, 10X); b) Insular pattern (H&E 40x); c) Solid sheets (H&E 40x).



[Table/Fig-6]: Microscopy: a) Microfollicular pattern (call Exner bodies) spaces filled with hyalinized material.(40x); b) Uniform, pale, round to oval nucleus with scant cytoplasm (40x); c) Round to oval nucleus shows coffee bean appearance of the nucleus (Nuclear groove) (H&E, 100x).

DISCUSSION

The GCT of ovary was first described by Rokitansky in 1855 as depicted in study by Diddle AW [3]. It is a rare ovarian tumour accounting for 1% of all ovarian tumours [1]. The age of presentation of GCT varies in a wide range from 21-64 years [4]. It is frequently seen in peri-menopausal age group and the mean age of presentation in the present case series was 44 years [5,6]. As the clinical presentation varies with age, abdominal pain and estrogenic manifestation such as abnormal uterine bleeding with endometrial hyperplasia was more frequent in reproductive age group and post-menopausal bleeding in older age group [5]. Androgenic manifestation was not observed in this cases series. Rarely endometrial carcinoma, can occur with GCT it was observed in one of the cases [4]. Elevated tumour markers such as β inhibin of sex cord tumour origin and CA125 in epithelial origin help in diagnosis and prediction recurrence in ovarian tumours. Pre-operative elevated serum CA 125 [5] has been observed in one of the cases which was associated with massive ascites [7]. It is predictive marker for recurrence but in this case series there were no recurrence observed. But contrary serum inhibin was elevated in all the present cases (100%) and serum levels were reduced post-surgery so it can be considered as marker for follow-up [8].

GCTs are usually unilateral and are typically solid and cystic with areas of haemorrhage and occasional solid with grey white homogenous cut surface. In this case series all 100% of the cases were of unilateral, with right-sided dominance (71.4%) [9,10]. A 78.5% of cases grossly solid cystic with haemorrhagic cut surface and in 21.3% of cases solid, grey white homogenous areas was observed. Rarely in GCTs preoperative or perioperative tumour capsule rupture occurs but it was not observed in any of the cases [Table/Fig-1]. GCTs have wide range of tumour size (4-22 cm), the authors observed the mean tumour size of 9 cm [11].

GCTs are usually diagnosed in early stage due to its evident clinical presentation. Surgery is the main line of treatment in early stage and adjuvant therapy advised in advanced cases; tumour with high-grade histology and with preoperative tumour rupture [9]. In the present series, 64.2% of cases underwent total abdominal hysterectomy of which in two cases lymphnode dissection was performed which was negative for metastasis. A 35.8% of cases underwent conservative surgery without lymphnode dissection [4,12]. Stage of the tumour is an independent prognostic factor. In this case series, most of the cases (92.9%) were of Stage-IA [4,6,9,13,14], one case presented as Stage-IIIC who received adjuvant chemotherapy and recurrence was not observed [7]. The findings in this case series highlight the lower stage of presentation and good prognostic characters of the tumour with no recurrence.

GCTs usually have varied architectural pattern and in this case series, on observation showed combination of microfollicular, diffuse sheet, solid nest, and trabecular pattern [4,15]. The call Exner bodies are considered characteristic feature of the tumour, and is reportedly present in 30-60% of these tumours. The call exner bodies were present in 57.1% of cases discussed in this series [5]. On the other hand, coffee bean appearance of the nucleus (nuclear fold) was seen in all cases in this case series [11]. Histopathological examination further revealed necrosis in very few cases 21.4% which was not associated with high nuclear grade in our study. GCTs have low mitotic index which directs towards low grade tumour, which was observed in this case series with low mitotic count of <4/10 HPF in 85.7% [4,16]. In one case along with AGCT of the ovary the contralateral ovary showed mature teratoma. GCTs have excellent prognosis, and low recurrence rate [17]. In the present series, most of the cases presented without capsule rupture, Stage-I, no necrosis and low mitotic index, on follow-up of all 14 cases does not show recurrence of malignancy [5].

CONCLUSION(S)

This cases series was prepared because of rare presentation of AGCT with low grade malignant potential but it has good prognosis if diagnosed at earlier stage. The findings restate characteristic estrogenic clinical manifestation, microscopic picture with call Exner bodies and nuclear groves, helps in early diagnosis. Rare necrosis, low mitotic count and lower stage of presentation had predictive and prognostic importance. Serum inhibin levels helped in tumour diagnosis conformation in this case series and the post-surgical values were used for recurrence follow-up. Further studies with a larger cohort and molecular markers will aid in the understanding of the tumour.

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PARTICULARS OF CONTRIBUTORS:
1. Associate Professor, Department of Pathology, Aarupadaiveedu Medical College and Hospital, Puducherry, India.
2. Assistant Professor, Department of Pathology, Mahatma Gandhi Medical College and Research Institute, Puducherry, India.
3. Associate Professor, Department of Pathology, Aarupadaiveedu Medical College and Hospital, Puducherry, India.
4. Professor and Head, Department of Obstetrics and Gynaecology, Aarupadaiveedu Medical College and Hospital, Puducherry, India.
5. Professor and Head, Department of Pathology, Aarupadaiveedu Medical College and Hospital, Puducherry, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dharmishtha Natvarlal Kapadiya,
277, 8th Cross, Anugraha Satellite Township,
Periyakatupallayam-605007, Tamil Nadu, India.
E-mail: dharmishthakapadiya@gmail.com

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