Case Reports

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Granulosa Cell Tumor of the Ovary: A Rare Case Report and Review of Literature

Priyanka Yoga Purini[1], Abhishek Raghava[2], Sharmila V[3], Suneel Rachagiri[4], Saranya Kondamudi[5]

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Abstract

Granulosa cell tumors (GCTs) are uncommon ovarian neoplasms that account for 2%-5% of ovarian malignancies. GCTs are of two types; one is the adult type seen among peri-menopausal women and another is juvenile type seen among prepubertal girls and in women aged less than 30 years of age. Adult granulosa cell tumors are more commoner than juvenile type. We present a case of GCTs of the ovary in post-menopausal women who presented to us with post-menopausal bleeding. On further evaluation, a solid mass is noted in the right ovary. Endometrial biopsy revealed disordered proliferative endometrium. She underwent staging laparotomy, and Intraoperatively, the right ovary is replaced with a 10x8 cm solid mass and capsular breech is noted. Histopathology of the specimen revealed a Granulosa cell tumor, stage IC2. Postoperatively, she received adjuvant chemotherapy with Carboplatin and Paclitaxel for 6 cycles and she is under follow-up.

Keywords: Post-menopausal, Endometrial hyperplasia, ovarian neoplasm, granulosa cell tumour, Adult granulosa cell tumor.

INTRODUCTION

Granulosa cell tumor is an ovarian sex cord stromal tumor that accounts for 70% of the tumors in this category, and it represents 2%-5% among ovarian malignancies[1]. These tumors are derived from granulosa cells of the ovarian stroma, which are hormonally active and, secretes estradiol. GCTs are classified into two types based on clinicopathological features. One is the juvenile type, which is seen among pre-pubertal girls and

Author's Affiliation: [1]Assistant Professor, Department of Obstetrics and Gynaecology, [2]Assistant Professor, Department of Medical Oncology, [3]Professor and Head, Department of Obstetrics and Gynaecology, [4]Assistant Professor, Department of Pathology, [5]Academic Junior Resident, AIIMS, Mangalagiri 522503, Andhra Pradesh, India.

Corresponding Author: Sharmila V, Professor and Head, Department of Obstetrics and Gynaecology, AIIMS Mangalagiri 522503, Andhra Pradesh, India.

E-mail: sharu_jipmer@yahoo.co.in

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in women younger than 30 years of age, and they represent only 5% of GCTs. Juvenile type of GCT are usually present at an early stage and associated with favourable prognosis[1]. Another type of GCTs is the adult type, which is most common and seen among peri-menopausal women. These adult GCTs also present in the early stage, but relapses tend to occur after many years of original diagnosis, seen in up to 25% of cases despite having had curative surgery[2,3]. The most important prognostic factor is the stage of the disease, with 10-year survival of 84-95% for stage I 50-65% for stage II, and to 17-33% for stages III and IV1. Patients with low risk stage I observation with follow up is sufficient. Patients with high risk stage I disease associated with large tumor size (≥10-15 cm), stage IC, poorly differentiated tumor, high mitotic index, or tumor rupture adjuvant chemotherapy to be considered because of the increased risk of relapse[1].We report a case of an adult type of granulosa cell tumor of the ovary stage IC2 in a post-menopausal woman who underwent staging laparotomy with adjuvant chemotherapy, and she is under follow-up.

CASE REPORT

A 78-year-old P2L2 postmenopausal woman presented to us with complaints of vaginal bleeding on and off for a period of 2 months. Her general examination was normal, and her vitals were stable. On abdominal examination, there was no ascites, and a cystic mass of 10 x 10cm was felt in the right iliac fossa, which was freely mobile with well-defined margins. The same mass was felt per vaginal examination with no nodularity on the pouch of Douglas. She has been evaluated further for postmenopausal bleeding and adnexal lesion. She underwent endometrial sampling which was reported as disordered proliferative endometrium. The MRI of the abdomen and pelvis showed 8.52 x 6.2 x 5.46 cm well-defined mixed solid cystic T1, T2 heterogenous signal intensity lesion noted in the right adnexa with internal T2 hyperintense cystic/necrotic areas. The right ovary was not seen separately from the lesion suggestive of right ovarian malignancy. She was further planned for staging laparotomy. Intraoperatively peritoneal wash was sent for cytology as there was no ascites, the right ovary was enlarged to 7x8cm solid mass with the capsular breach, left ovary and both tubes were normal (Fig. 1, 2). The total hysterectomy with bilateral salpingo-ophorectomy along with omentectomy was done. Pathological analysis of the specimen was granulosa cell tumor-adult type with involvement of surface of ovary, disordered proliferative endometrium, cervix showed chronic cervicitis, omentum, fallopian tube and the other ovary was free of tumor(stage IC2) the peritoneal wash was negative for malignancy. She received adjuvant chemotherapy with carboplatin and paclitaxel 6 cycles in view of stage IC2 ovarian cancer.

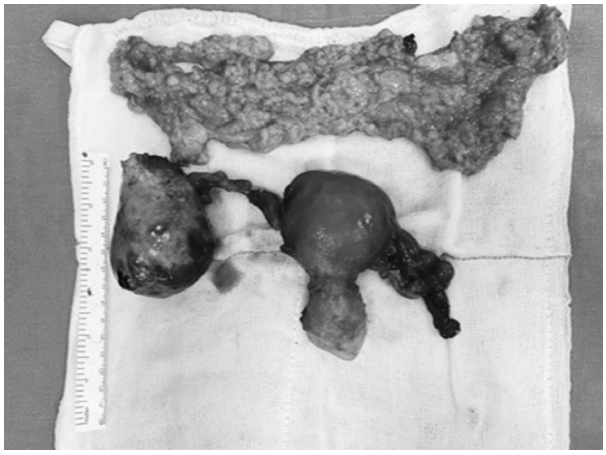

Fig. 1: Image of gross specimen showing uterus with right solid ovarian mass, left ovary is atrophic, bilateral tubes and omentum appears normal

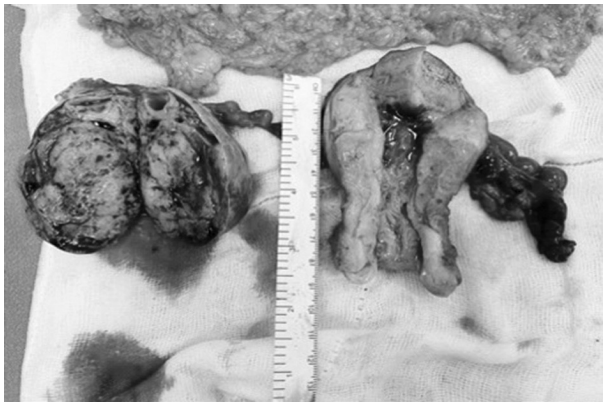

Fig. 2: Image showing cut section of enlarged uterus and ovarian mass

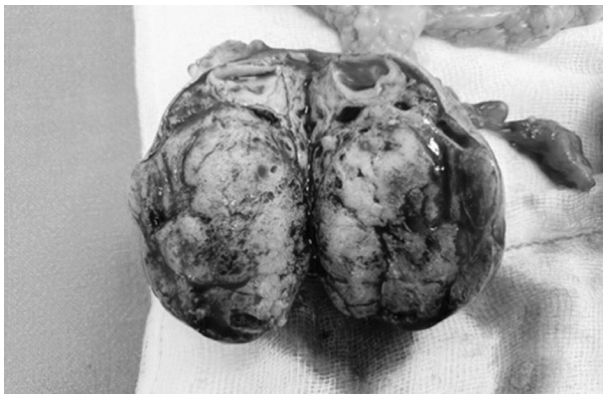

Fig. 3: Image showing cut section of the granulosa cell tumor of the ovary in which predominantly solid areas with very few cystic areas are seen

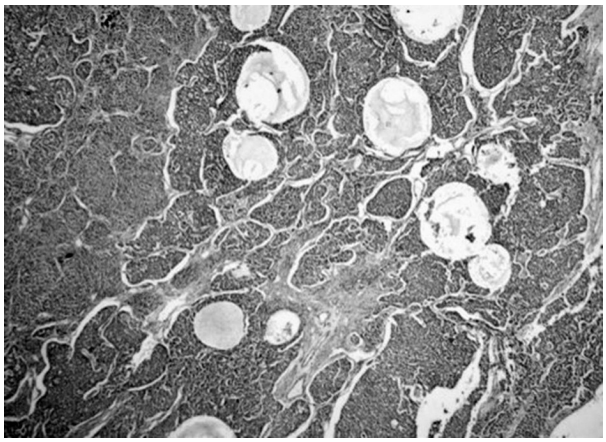

Fig. 4: HPE image showing the tumor cells arranged in diffuse, trabecular, insular and macrofollicular growth patterns with intervening stroma

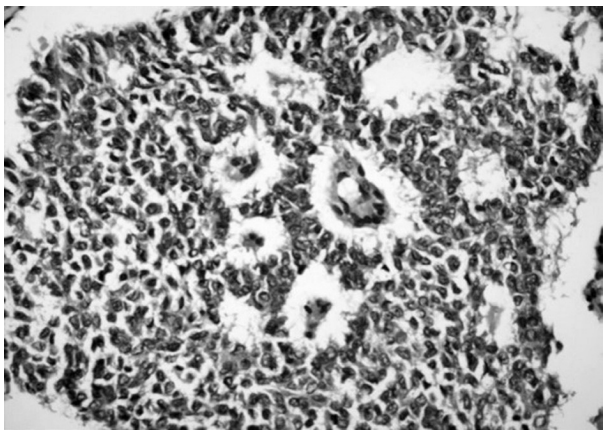

Fig. 5: Microfollicular pattern (call-exner bodies)

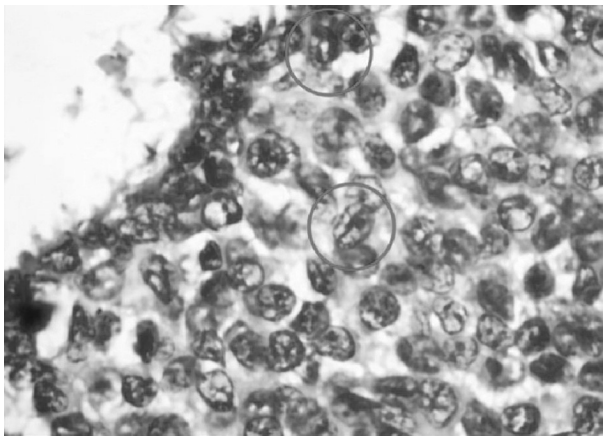

Fig. 6: Oil immersion view (100x) to highlight the nuclear grooves. The tumor cells having round to oval nuclei, irregular nuclear membranes and scant cytoplasm. Mitosis is low

DISCUSSION

Granulosa cell tumors are uncommon ovarian neoplasm that represents 2%-5% of all ovarian malignancies. GCTs are sex cord stromal tumors, they contribute around 70% of this category of ovarian tumors[1]. Based on clinicopathological characteristics, GCTs are classified as juvenile type and adult type. Juvenile type comprises 5% of granulosa cell tumors and is usually seen among pre-pubertal girls and in women less than 30 years of age. The most common presenting symptoms are abdominal pain, abdominal distention, and mass per abdomen. These tumors are hormonally active secreting estradiol, leading to hyperestrogenism. In prepubertal girls, these tumors cause isosexual precocious peudo-puberty, bleeding per vaginum, and irregular menstruation. Neoplastic granulosa cells secrete androgens, leading to virilization and hirsutism[4]. The mean age at the time of diagnosis is 13 years and 80% of juvenile granulosa cell tumors occur below the age of 20 years. Ten percent of cases are present during pregnancy. CA-125, Inhibin-B and serum anti-mullerian hormone are found to be elevated in Juvenile GCTs[5]. Adult GCTs are the most common compared to juvenile GCTs and contribute around 95% of GCTs[6]. Adult GCTs are seen among perimenopausal and post-menopausal women. These presenting complaints of Adult GCTs are similar to Juvenile GCT like abdominal mass, abdominal distention, and abdominal pain. These women present with post-menopausal bleeding or menstrual irregularities. In our case, she is a post-menopausal woman who presented with post-menopausal bleeding and, on endometrial sampling, revealed disordered proliferative endometrium. The gross appearance of both Juvenile GCTs and Adult GCTs are similar with solid and cystic components. In AGCTs, cystic (30.3%), solid (27.8%) or solid, and cystic (41.7%), while JGCTs show similar gross features, which are cystic (14%), solid (37%) and solid and cystic (45%). In our case, the tumor is completely soild on the cut section. The MR imaging features of GCTs are a sponge-like appearance with solid areas of intermediate signal intensity and numerous cystic spaces on T2-weighted MRI images, and hemorrhagic foci of high signal intensity on T1-weighted MR images[7]. Women with GCTs can have endometrial hyperplasia or uterine enlargement due to hyperestrogenism. Recent studies confirmed that serum inhibin is not a specific tumor marker for the diagnosis of GCTs. Immunohistochemical analysis also confirmed that not all patients with GCT will have an increase in inhibin levels, and patients with Epithelial ovarian cancers also show elevated serum inhibin levels[8]. Therefore, to consider serum inhibin in post-menopausal as a tumor marker for GCT is contradictory[9]. Serum AMH is a specific tumor marker for granulosa cell

tumor (GCT), with a sensitivity ranging between 76 and 93%. Serum AMH can be used as a marker during post-operative follow-up for disease recurrence[3]. Elevated serum estradiol levels are seen in women with GCTs, but it is not a reliable tumor marker. Approximately 30% of patients with GCTs will have normal serum estradiol levels[1]. FOXL2 gene somatic missense mutation is a pathognomic of Adult GCTs of the ovary. FOXL2 is involved in the pathogenesis of Adult GCT through multiple pathways[11]. FOXL2 mutation is the major driving force of Adult GCT. Therefore, FOXL2 targeted therapy may offer unprecedented potential to eliminate oncogenes and prevent resistance to conventional chemotherapy[3]. Histologically Adult GCT exhibits specific patterns such as high-grade and low-grade differentiated patterns. The high-grade differentiated histological pattern usually presents in several forms, including microvesicles, trabecular, island, tubular, and hollow tubular forms, more commonly seen with Adult GCT. Call-Exner bodies, the most typical histological pattern of microbubbles, play an important role in histological diagnosis. The low-grade differentiated pattern usually shows a watered-silk or gyriform pattern, which refers to a diffuse distribution and is known as the sarcomatoid type. The well-differentiated and poorly differentiated patterns contain round to oval, pale cells, and the nucleus is a typical coffee bean groove. There is no issue of misdiagnosis between Adult GCT, undifferentiated carcinoma, adenocarcinoma, and carcinoid tumors due to its specific coffee bean nuclear appearance. Surgery, i.e., staging either by laparotomy or laparoscopy, is the mainstay of treatment for GCTs both adult type and juvenile type. As juvenile GCTs are seen among young and adolescent girls where fertility-sparing is required, in these girls, removal of a diseased ovary with contralateral ovarian biopsy in case of any suspicion and completion with surgery is planned once she finishes her family. Management of Adult GCTs depend on the FIGO staging and require complete staging which includes total abdominal hysterectomy, bilateral salpingo-ophorectomy with infracolic omentectomy. In the case of recurrent GCTs, and debulking surgery are required. Platinum-based combination chemotherapy like epithelial ovarian cancer is recommended due to its rare occurrence.

CONCLUSION

The Granulosa cell tumor of the ovary is an uncommon ovarian sex-cord stromal tumor. Juvenile type is seen among young females, where as adult type is seen among the perimenopausal age group. As it is a functional tumor, it secretes estradiol, leading to hyper-estrogenism. Serm AMH is a specific tumor marker for granulosa GCTs. Recent studies show that Serum inhibin B is not specific tumor marker for GCTs. Approximately 30% of the individuals with GCTs will have normal estradiol levels. The majority of the patients with granulosa cell tumors of the ovary are present at the early stage. Surgery is the primary treatment modality for granulosa cell tumors. Advanced stage and presence of residual disease were associated with inferior survival. Prognostic factors include the stage of the tumor. Others include mitotic activity and nuclear grade. Hence, staging and histopathology help prediction of survival.

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