CASE REPORT

Granulosa Cell Tumour – A Rare Presentation at Age Twenty

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ABSTRACT

Granulosa cell tumor is a rare type of ovarian tumor, which arises from sex cord stroma. Histologically this tumor has two types and is named according to the common age group they affect; adult granulosa cell tumor (AGCT) and juvenile granulosa cell tumor. AGCT constitutes 2-5% of all ovarian cancers. Mostly present in women of age > 40 years. In this case report, we discussed the role of conservative surgery in young adult reported with granulosa cell tumor. An unmarried teenage girl presented at a private tertiary care hospital with abdominal pain and abdominal distention. Radiological examinations suggested a mass originating from the right ovary for which laparotomy was done and a ruptured cyst was found near the right ovary with a mass adherent to surrounding peritoneal viscera. Right ovarian cystectomy along with omental biopsy and left ovarian biopsy was performed. Rare presentation of this tumor will help clinicians to not categorize the type histologically with the age group.

Keywords: Granulosa Cell Tumor; Ovarian Mass; Laparotomy.

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INTRODUCTION

Majority of adult-type granulosa cell tumor cases present in early stages. Stage I has a favorable outcome and a low rate of recurrence as compared to late stages[1]. These tumors are unilateral with no side predominance. Women of reproductive age reported with hirsutism and menstrual irregularities such as amenorrhea, intermenstrual bleeding and menorrhagia due to hormones produced by tumor; estrogen and androgen. Some patients also report abdominal distention, acute abdominal pain, nausea, and vomiting due to ovarian torsion or hypotension. FOXL2 mutation determination is recommended for primary diagnosis[2]. Granulosa cell tumors are also associated with endometrial hyperplasia or carcinoma[3]. The study will not only discuss the different aspects of granulosa cell tumor in young adult but also strengthen the role of conservative surgery in management of young adults suffering from granulosa cell tumor.

CASE REPORT

A 19-year-old unmarried female with no known comorbidities presented to Out Patient Department (OPD) of Ziauddin University Hospital with complaints of lower abdominal pain for past two weeks and abdominal distention for past two weeks. She also reported to have had irregular menstrual cycles for last two years and had taken hormonal therapy for this. On abdominal examination, slight distention was noted with inverted umbilicus, abdomen was soft and slightly tender with a palpable mass below the umbilicus.

Initially, Ultrasound Pelvis (Figure1a) was performed which revealed a large multilobulated solid lesion measuring 16.0x10.9cm with multiple cystic areas in mid of the pelvis. It also suggested the presence of mild to moderate ascites in the abdominopelvic cavity.

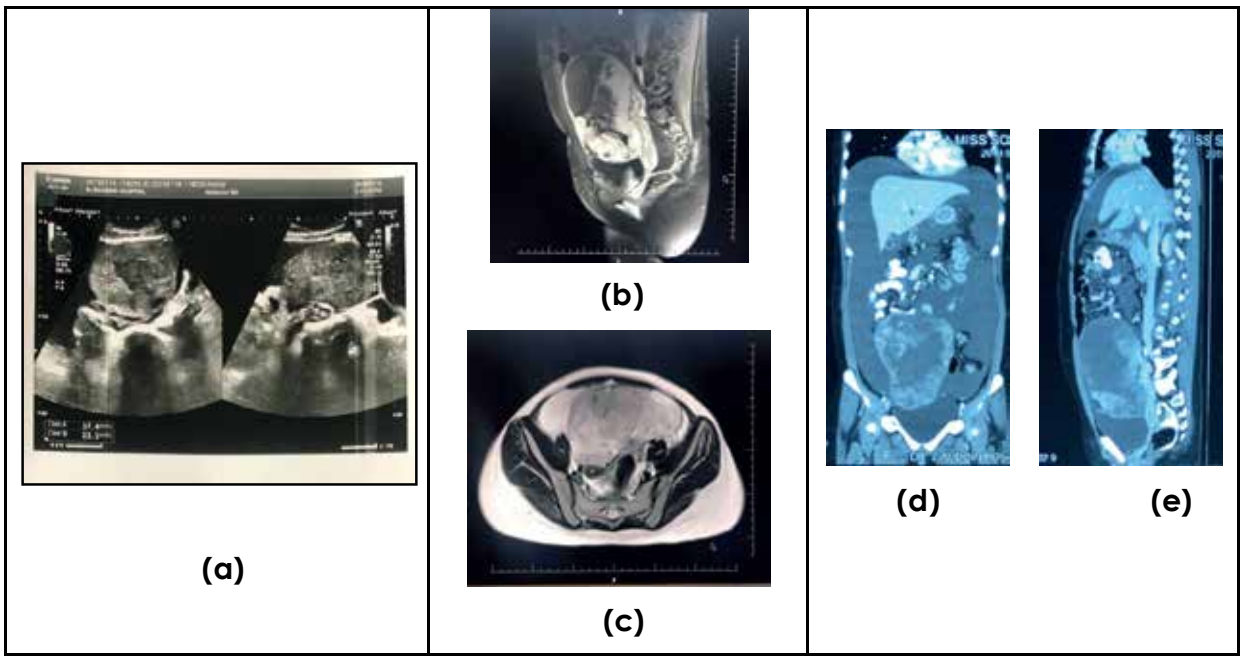

Figure 1: (a) Ultrasound of Pelvis showing multi lobulated solid mass in mid pelvis; (b, c) MRI of Pelvis showing oval shaped mass towards right adnexa; (d, e) CT scan of the abdomen showing solid mass extending to abdominal wall anteriorly, compressing the uterus posteriorly with moderate to severe ascites in abdominopelvic cavity.

Further evaluation of the disease was made by Magnetic resonance imaging (MRI) of Pelvis with contrast (Figure 1b, c) which showed a large well defined oval-shaped capsulated solid mass measuring (16.5 x 10.1 x 13.2)cm in craniocaudal (CC), anteroposterior (AP) and transverse (TV) dimensions in the center of the pelvis with predominant bulk towards right adnexa. Both ovaries were not separately identified completely from the lesion and probably the lesion was arising from the right ovary. Areas of necrosis and hemorrhage were noted inside the lesion. Omental thickening anterior to abdominal wall and free fluid in lower abdomen and pelvic peritoneal cavity was also noted. Normal size anteverted uterus with normal endometrium was seen.

The computerized tomography (CT) scan of whole abdomen (Figure 1d, e) was done which confirmed the previous findings. Anteriorly the mass is extending towards anterior abdominal wall. Posteriorly extended mass is abutting and compressing the uterus. Posterolaterally, mass is abutting the terminal ileum on the right side and cecum on the left side of the sigmoid colon. Inferiorly the mass is abutting the dome of urinary bladder. Superiorly it is abutting and compressing the adjacent bowel loops. The mass is abutting and compressing the right ureter. Both ovaries are not separately visualized. Moderate to severe ascites seen in abdominopelvic cavity. Few lymph nodes of less than one centimeter are seen in abdomen, para-aortic and aortocaval location.

Her basic workup investigations were done which showed (Table1) which shows hemoglobin 10.6 g/dl, total leucocyte count 9.80 x 10^9/L platelets 364000 platelets/µL, cancer antigen-125 1697 U/mL, lactic acid dehydrogenase 195 U/mL, beta human chorionic gonadotropin negative and alpha-fetoprotein 2.03 ng/mL (Table 1).

Table 1: Investigation profile of a patient.

Variables	Results	Reference Value
Hb	10.6	12.0 -15.5g/dl
TLC	9.80	4.5 -10.5 x10^9/L
PLT	364	150 -450
CA125	1697	<46 U/mL
LDH	195	100 -190U/L
bHCG	-VE	-
AFP	2.03	<10ng/mL

Hb: Hemoglobin; TLC: Total leucocyte count; PLT: Platelets; CA: cancer antigen; LDH: Lactic Acid Dehydrogenase; bHCG: Beta human chorionic gonadotropin; AFP: alpha-fetoprotein.

Patient was admitted and Laparotomy (Right ovarian cystectomy +Omental biopsy +Left ovarian biopsy + Adhesiolysis + Superficial bladder repair) was performed. Intraoperative findings (Figure 2a, b): right ovarian cyst, glistening surface, torsion of ovary, ruptured cyst adherent anteriorly to bladder.

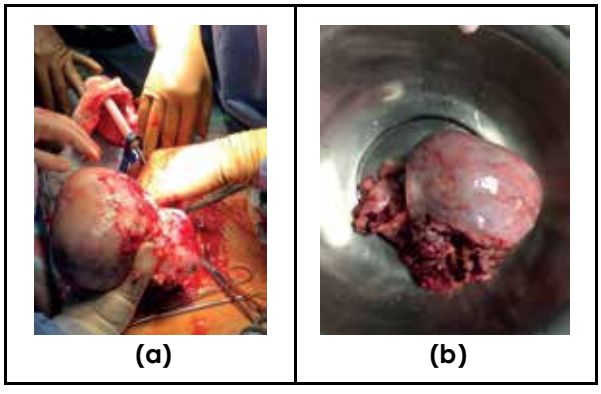

Figure 2a, b: Intraoperative findings showing right ovarian cyst with glistening surface, it was ruptured adherent anteriorly to bladder and right fallopian tube stretched out over cyst.

Frozen section was taken and sent for histopathology studies, showed adult granulosa cell tumor and calretinin was strongly positive on immuno-histochemistry. Case was discussed and further plan for endometrial sampling and chemotherapy was recommended. Endometrial biopsy showed disordered proliferative endometrium.

DISCUSSION

Granulosa cell tumors are uncommonsex stromal neoplasms with a slow progressing nature[4]. The granulosa cells produce the sex steroid and due to high levels of estrogen, cause hyperestrogenism[5]. Granulosa cell tumors are mainly of the following two types: Adult tumor and Juvenile tumor. We make this distinction on the basis of clinical and histopathological characteristics[6]. Adult type being the more common one and accounting for 95% of all granulosa cell tumorsand 2%- 5% of all ovarian malignancies[7].

The juvenile type as the name suggests is the form that affects mainly the prepubertal girls and women of age < 30 years while the adult type shows the highest incidence in ages of 50 to 55 years (postmenopausal period). It is the less rare type and represents about 5% of all Granulosa cell tumors[5]. Granulosa cells are characterized by small round and pale cells with characteristic nuclei of coffee beans. When these cells are well differentiated they have different patterns that are as follows: micro follicular, macro follicular, solid-tubular, trabecular, insular and hollow tubular[5].

Although any patterns may be observed, but most commonly observed is the micro follicular pattern. These cells are characterized by Call- Exner bodies[8]. These are small rings made up of granulosa cells, which either surrounds the shrunkennuclei or eosinophilic fluid material[5]. In the case report, the girl is 20 years of age and she presents with a tumor identified by the histopathology report as the adult type. The adult form, which is a low-grade malignant sex cord-stromal tumor, occurs occasionally in young children. Therefore, for our 20-year-old patient to have this marks a rare case. Patients will usually present with abdominal pain, distention and irregular bleeding (adult type: postmenopausal bleeding) due to secretion of estradiol[4].

Abnormal uterine bleeding and irregularities in the menstrual cycle are more commonly observed in adult women of reproductive age who are hormonally active and suffering from granulosa cell tumor. Another common finding is endometrial hyperplasia, which is again due to high levels of estrogen. Tumor torsion ovary may present at times, which causes acute abdominal pain. Tumor rupture is also seen in about 10% cases causing manifestations such as acute pain in abdomen, distention and hypotension because of hemoperitoneum[5].

Unfavorable factors include advanced stage (most important), large size (>15cm), bilaterally present tumor and tumor rupture, which can then cause acute abdominal pain (6-10%). Morphological features including nuclear grooves, positivity of immunohistochemical Stain Inhibin, negative EMA and P53 support granulosa tumor, which may show necrosis. The imaging characteristics of both types are non-specific so difficult to distinguished easily from other types of ovarian cancers. Computed Tomography scans with a diffused pattern may also be mistaken in diagnosis of poorly differentiated carcinoma.

Circulating biomarkers are most commonly and accurately used for diagnosis of granulosa tumor such as; anti-Mullerian and Inhibin B. In such type of tumors FOXL2 gene is mutated at missense point 402->G(C134W), resulting in increased proliferation along with enhanced surviving ability of granulosa cells which in turn encourages the hormonal changes[9]. Histologically adult granulosa cell tumor identification is a difficult task. Therefore, FOXL2 mutation testing is very helpful in detecting problematic cases. It has shown that 97% of adult granulosa cell tumorsshowed mutation of FOXL2 gene[4].

Staging of tumors is one of the most important features that help in establishing the prognosis oftumors[9]. As staging of tumors increase, the survival percentage drastically decreases. A 10-year survival rateof stage I tumor is 84-95%, 50-60% for stage II tumors and a further 17-33% for stage III and IV[10]. FIGO staging system is the preferred staging system in granulosa cell tumors and helps in identification of patients who are at risk or those who require therapy. Out of all its subtypes, Figo

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subtype 1C is found to be predictive of recurrence. When treated it can result in disease-free survival in early-stage patients of adult granulosa cell tumors (AGCTs)[7].

AGCTs are less likely to be malignant compared to the juvenile type but they have a higher chance of recurrence hence, a follow up is highly required. It is also very important to know that follow up is essential because when relapse occurs it is more aggressive in nature with poor outcomes. When assessing via pelvic examination, the most common finding is a tumor mass. It can then be subsequently confirmed with imaging techniques[4].

The primary treatment for granulosa cell tumors should be complete tumor resection. In this case, chemotherapy is planned for the patient, which is usually a combination of anticancer agents including; bleomycin, etoposide, cisplatin; etoposide/cisplatin and paclitaxel and carboplatin. Relapse rates are as high as 31% so regular follow-ups are very important whereas pelvis is the most common site of recurrence. If relapsed, there is no standard approach for management. Surgery may possibly provide long-term control for localized disease[4].

If a more traditional approach is adopted then a unilateral salpingo-oophorectomy is suggested in patients of reproductive age having stage I tumor, whereas total abdominal hysterectomy and bilateral salpingo-oophorectomy is suggested in patients who have reached menopause or for those who have a higher grading of the tumor. It is hence emphasized that stage of the AGCT is a very important prognostic factor correlated with risk of prolapse[4].

AGCT can also affect younger women so fertility preservation is another important problem in management AGCT. However, the importance of fertility surgery is unclear. Few studies report the association of fertility surgery with a higher rate of recurrence and decreased rate of survival[7].

CONCLUSION

It was concluded that conservative surgery could play an effective role in management of young adults reported with granulosa cell tumor. Further investigated that majority of the patient with granulosa cell tumors of the ovary present in early-stage and have favorable prognosis. In A prospective multi-centric trial is needed to address the role of adjuvant therapies for optimal management of these rare neoplasms.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

PATIENT CONSENT

Patient consent was taken before starting the procedure and for publishing.

AUTHORS' CONTRIBUTION

RH gave the idea; SC supervised the study; MA collected the data; RR wrote the manuscript and finalized it and SN conducted literature search.

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