

## A 17 year old girl with gradual swelling of lower abdomen

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### Article Info

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### Presentation of Case

*Dr. Sayada Fatema Khatun:* A 17 year old girl presented at the outpatient department with the history of gradual swelling of lower abdomen, early onset of menstruation (precocious puberty) at the age of 7 years followed by secondary amenorrhea for 10 years, growth retardation and breast atrophy. She also complained that her secondary sexual characteristic did not develop. She had no family history of growth retardation or precocious puberty. Her breast showed infantile growth. She had no history of fever, abdominal pain, alteration of bowel habit, weight loss, or loss of appetite. On examination, she was afebrile and vitally stable. Her height was three feet and nine inch (severely stunted) and underweight (25 kg). Per vaginal examination revealed no pubic hair. No lymph node was enlarged. Neurological, cardiovascular and other systems revealed no abnormality. She was intelligent. Per abdominal examination revealed a lump in the hypogastrium about 16 weeks in size, firm in consistency, non-tender, smooth surfaced, well defined margin, and round in shape. There was no ascites. Her serum estrogen and testosterone levels were increased. Other hormones like follicle stimulating hormone, luteinizing hormone, prolactin, dihydroepiandrosterone and progesterone were within the normal limit. Karyotyping and intravenous urogram were normal. Ultrasonography findings showed right adrenal mass (3 x 4 cm) with uterine myoma (7.4 x 6.3 cm). CT scan of the whole abdomen showed the same result. After evaluating the clinical data, physical findings and investigation results, the case was provisionally diagnosed.

### Provisional Diagnosis

Sex cord stromal tumor

### Differential Diagnosis

*Dr. Jannatul Ferdous:* Patient Presented with lower midline swelling and secondary amenorrhea. So, there may be a differential

diagnosis of uterine myoma.

#### Uterine myoma

In this case, clinical features, ultrasonography and CT scan findings indicate it as a case of uterine myoma. But her hormone profiles showed increase serum estrogen and testosterone levels. In juvenile granulosa cell tumor, there may be associated uterine myoma or endometrial hyperplasia or abnormal uterine bleeding due to excessive estrogen level. The ultimate final diagnosis is done by histopathological analysis.

*Dr. Khairun Nahar:* As there was increased level of serum testosterone and estrogen, other differential diagnosis may be granulosa cell tumor, thecoma, fibroma, androblastoma and gynandroblastoma. However, histopathology of Call-Exner bodies, nuclear grooves and immunohistochemistry markers help in ruling out the differentials.<sup>1,3</sup>

#### Granulosa cell tumor

Granulosa cell tumor is an uncommon neoplasm. It is two types: Adult and juvenile form. Adult form is slowly progressive and diagnosed in early stage. Juvenile form is more aggressive. Long term follow up is necessary in both types because of recurrences. Histopathology and immunohistochemistry are necessary in both these types for the final diagnosis. Both serum estrogen and testosterone levels are increased in granulosa cell tumor.

#### Ovarian thecoma

Thecal component was seen along with granulosa cell tumor but it is necessary of the presence of more than 25% of thecal cells in case of thecoma. Thecoma is a benign condition with good prognosis.<sup>4</sup>

The immunohistochemistry markers valuable in this entity are the vimentin, CD99 and inhibin.<sup>2</sup>

#### Fibroma

Fibroma is usually observed in post-menopausal women. It is derived from the stromal cells and thecoma is similar to fibroma. In fibromas, there is increased cellularity and pleomorphism.



Table I

## Laboratory findings

Investigation	Patient's value	Reference value
Hemoglobin (g/dL)	12.7	
Erythrocyte sedimentation rate (mm/1 <sup>st</sup> hour)	30	
Random blood sugar (mmol/L)	4.7	
Platelet (x 10 <sup>9</sup> /L)	350	
WBC (x 10 <sup>9</sup> /L)	8	4-10
Neutrophil (%)	56	40-80
Lymphocyte (%)	35	20-40
Monocyte (%)	4	2-10
Serum albumin (g/L)	40	35-50
Serum bilirubin (mg/dL)	0.3	0.3-1.2
TSH (IU/mL)	3.2	0.47-5.01
FT <sub>4</sub> (ng/mL)	1.3	0.8-1.8
17- OH progesterone "O" (ng/mL)	1.7	5-20
Serum testosterone (ng/mL)	151.9	15-70
Serum estrogen (pg/mL)	1194.2	27-123
Serum prolactin (ng/mL)	11.6	1.39-24.2
luteinizing hormone (IU/L)	1.0	5-15
Follicle stimulating hormone (IU/L)	1.1	3-20
DHEA (ng/mL)	5.3	2-10
Serum electrolyte (mmol/L)	Na <sup>+</sup> : 135; K <sup>+</sup> : 4; Cl <sup>-</sup> : 102	
Serum creatinine (mg/dL)	0.55	0.5-1.2
Serum alanine aminotransferase (IU/L)	14	<40
HbsAg	Negative	
Urine R/E	Normal	

**Androblastoma**

Sertoli-Leydig cell tumor is rare (about <0.5% of all ovarian tumors and less than 5% of all sex cord stromal tumor). This tumor produces androgen which causes defeminization, breast atrophy and amenorrhea followed by masculinization (50%). Due to masculinization, there is male type distribution of hair, hoarseness of voice, breast atrophy, hirsutism, baldness and clitoral enlargement. Our patient had only breast atrophy and amenorrhea.

**Gynandroblastoma**

This is a very rare type of tumor. It contains both granulosa cell (estrogenic) or Sertoli-Leydig cell (androgenic) types. Usually it is a benign tumor.

**Discussion**

Rokitansky described granulosa cell tumor first time in 1855.<sup>3</sup> According to their appearance near the granulosa cell and ovarian follicles, WHO describes them. They occur in peri- and post-menopausal women aged between 50 to 55 years. Another pick frequency is pre- pubertal age.<sup>6,7</sup> Abdominal pain (30-50%), abdominal distension due to mass and hormonal events such as 40% develop irregular menstruation, inter-menstrual bleeding or amenorrhea.<sup>8</sup> However, clinical examination is very important for asymptomatic patient.<sup>9</sup> About 66% patients show endocrine manifestations. These manifestations are due to excess secretion of estrogen and androgen. This explains why endometrial adenocarcinoma are frequently associated with granulosa cell tumor (5-35%).<sup>7,8,10</sup> Present of pseudopuberty is a characteristic form of juvenile granulosa cell tumor.<sup>11,12</sup> Galactorrhea or breast atrophy may complete the clinical presentation.

*Dr. Ferdous:* The diagnosis is confirmed by histological analysis. There are five subtypes of adult form. Among which, the most common subtype is the microfollicular type which is characterized by Call-Exner bodies and cores of coffee bean.<sup>13,14</sup>

In the juvenile form, the architecture is lobulated, Call-Exner bodies are rare and there is increase signs of luteinization.<sup>15</sup>

The main immunohistochemical markers expressed by these cells are vimentin, CD99 and  $\alpha$ -inhibin.<sup>3</sup>

*Dr. Khatun:* The traditional treatment modalities are complete excision of the tumor with unilateral salphingo-ophorectomy in case of fertility preservation. Total abdominal hysterectomy with bilateral salphingo-ophorectomy if patient's family is completed. Sometimes chemo- or radio-therapy may be needed after surgery.<sup>1,2,16</sup>

There is no standard regimen for adjuvant treatment, but it is usually recommended for adult granulosa cell tumors or for patient at high-risk.<sup>17-19</sup>

This patient is re-commended for adjuvant chemotherapy at tumor board in this university. Before that patient was advised for estimating the level of inhibin, estradiol and complete blood count.

*Dr. Nahar:* Laparotomy was done which was followed by myomectomy with right sided salphingo-ophorectomy with infracolic omentectomy with surgical staging.

**Operative findings**

The uterus of about 18 weeks in size, a large fibroid was in the posterior uterine wall (5 x 6 cm) in size (Figure 1), solid in consistency, capsule intact,

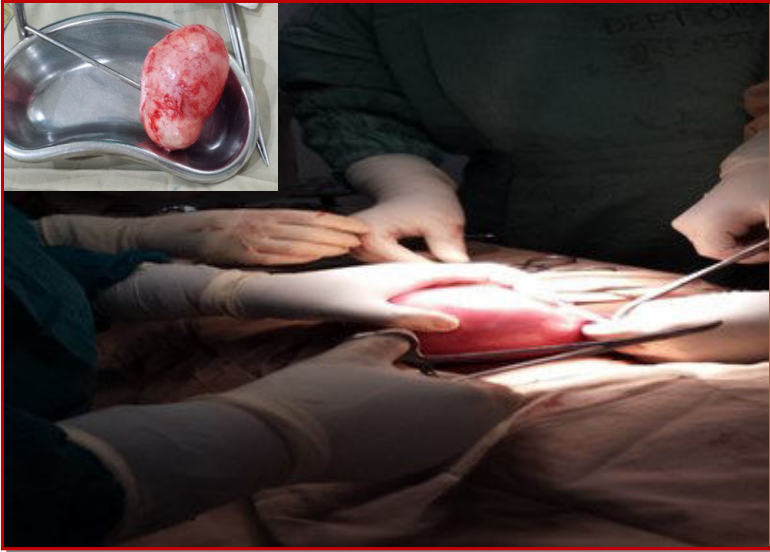


Figure 1: Right sides salpingo oophorectomy was done due to enlarged right ovary. Uterine myoma was resected (inset)

smooth surfaced. The right ovary was enlarged, size about (5 x 4 cm) in size, irregular surface, hard in consistency, capsule were intact, no ascites. Myomectomy was done and sent for histopathology. Complete abdominal exploration was done. Left ovary was streak. There was no deposit. Both sided pelvic lymph nodes were not enlarged. Peritoneal washing was taken for cytology.

Histopathological findings show that the peritoneal washing was negative for malignant cells. The right ovary showed granulosa cell tumor with foci of pleomorphism with few mitosis (Figure 2). The resected uterus was liomyoma. The omentum was free of tumor.

*Dr Ferdous:* What is the recurrence rate of juvenile granulosa cell tumor?

*Dr. Khatun:* Juvenile granulosa cell tumor is rela-

tively benign and the survival rate is as high as 97% while the chance of recurrence is higher in adult granulosa cell tumor.

*Dr. Latifa:* What are the chemotherapy agents prescribed for this patient?

*Dr. Khatun:* The most widely used chemotherapy regime are BVP (bleomycin, vinblastin, cisplatin) or BEP regime substitute etoposide for vinblastin.<sup>20</sup>

The hormonal therapy is megestrol and LHRH agonists also has a good responses, specially for recurrent cases.<sup>21, 22</sup>

About 70% of granulosa cell tumor secretes the estrogen which is responsible for precocious puberty in juvenile granulosa cell tumor while in case adult granulosa cell tumor, it is responsible for the endometrial hyperplasia, endometrial carcinoma and abnormal uterine bleeding.

Our patient complains of precocious puberty, breast atrophy and stunted growth. Unlike adult granulosa cell tumor, fewer Call-Exner bodies are seen in the juvenile granulosa cell tumor. Morphologically and radiologically it is not possible to differentiate between the two verities.

*Dr. Sabera Khatun:* How will you do the final diagnosis of this patient?

*Dr. Khatun:* Both clinical and histopathological guidelines are needed to correctly subcategorize granulosa cell tumors into types and the age cannot be considered as the definite criterion.

*Dr. Fahmida:* What are the serum tumor markers raised in case of juvenile granulosa cell tumor?

*Dr. S. Khatun:* The serum tumor markers raised in granulosa cell tumor are estradiol, inhibin, antimullerian hormones. C-125 is not correlated with the tumor progression.<sup>14</sup>

*Dr. Nusrat:* What are the prognostic factors of juvenile granulosa cell tumor?

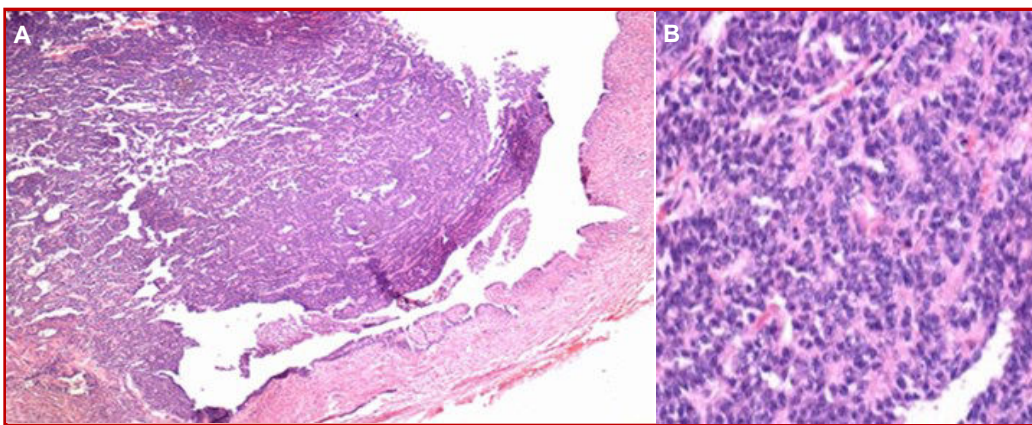


Figure 2: Multi-layering of the lining epithelium which is present in juvenile granulosa cell tumor (A); Many nuclei show irregular nuclear margins and a few show grooves (B). Call-Exner bodies are seen

*Dr. Nahar:* Staging is a traditional paramount for prognosis. Intraperitoneal disease, tumor size, patient age, histologic grade of differentiation, mitotic activity and nuclear atypia are the other prognostic factors of granulosa cell tumor [3,16,23,24](#)

*Dr. Sabiha:* What are the survival rates of this patient?

*Dr. Khatun:* Survival rates of this patient after 10 years for stage 1, 2, 3, and 4 are 87.2, 75, 20, 0% respectively [2,15,25](#)

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### Final Diagnosis

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Juvenile granulosa cell tumor of right ovary with uterine myoma

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