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# Juvenile granulosa cell tumor diagnosed in 6-month-old infant with precocious puberty<sup>☆</sup>

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## ABSTRACT

Juvenile granulosa cell tumor is a rare tumor diagnosed in children, which can present with precocious puberty. We have reported a case of a 6-month-old female patient who presented with precocious puberty. Abdominopelvic imaging revealed a large mixed cystic and solid mass, with internal solid enhancement, and restricted diffusion. At surgery, mass was confirmed to arise from the left ovary, and histopathology confirmed juvenile granulosa cell tumor. We provide a literature review of juvenile granulosa cell tumor and discuss imaging characteristics of this diagnosis.

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## Introduction

Juvenile granulosa cell tumors are rare ovarian neoplasms diagnosed in the pediatric population. These tumors are commonly clinically significant due to their hormone secreting properties, resulting in symptoms of precocious puberty. While primary imaging characteristics are non-specific ranging from cystic to solid masses, secondary characteristics such as uterine enlargement, endometrial thickening, and breast bud development abnormal for age can be helpful in diagnosis. In this article, we will present a case of juvenile granulosa

cell tumor diagnosed in infancy, as well as our hypothesized effects on the affected ovary.

## Case summary

A 6-month-old female was referred to the Endocrinology clinic for precocious puberty. The mother of the patient reports a normal pregnancy and delivery. Patient was born at term by spontaneous vaginal delivery and has no other health problems. Per mom, patient has coarsening of arm and leg hair

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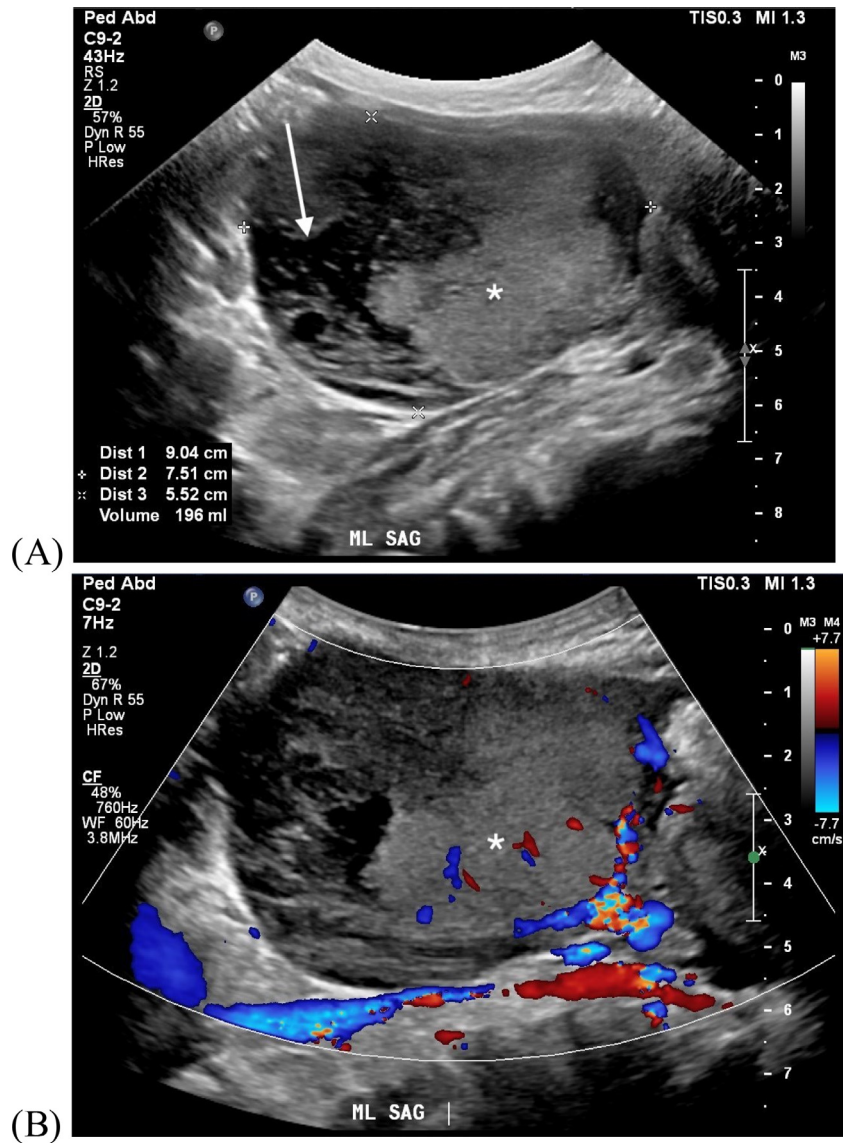
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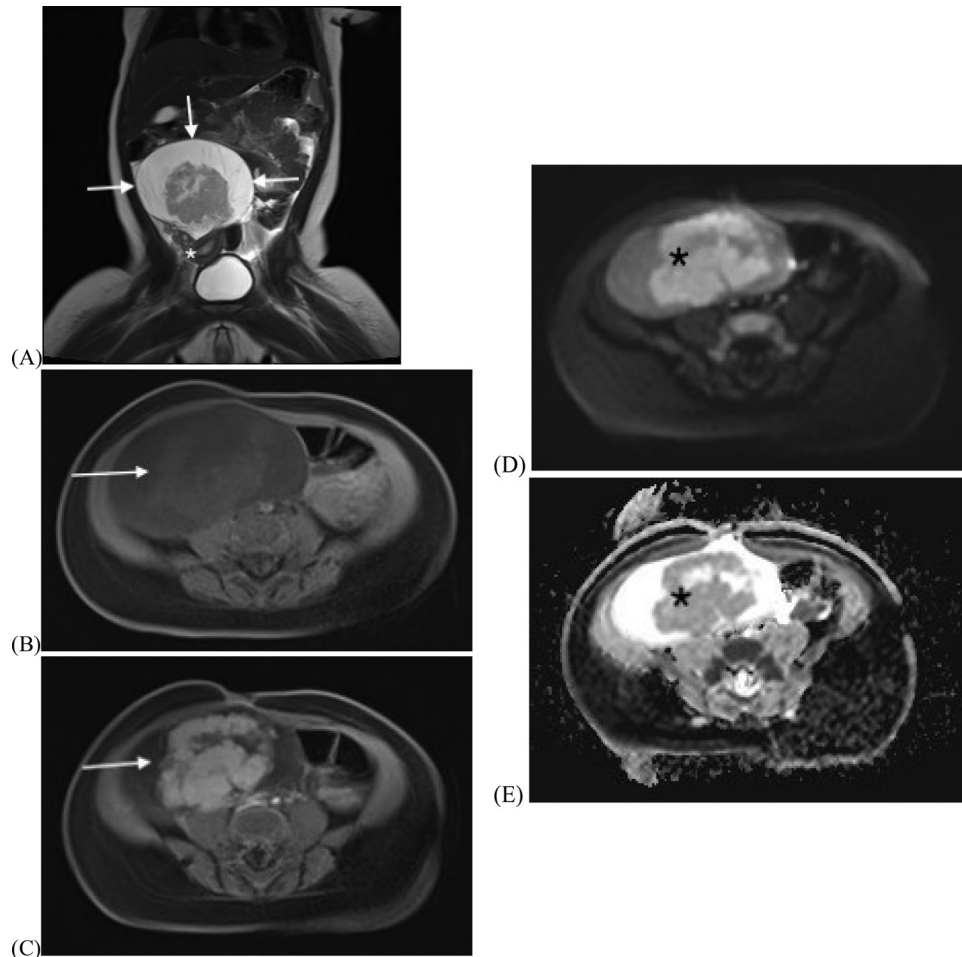
**Fig. 1 – Ultrasound of pelvic mass. (A) Grayscale ultrasound of mixed cystic (white arrow) and solid (white asterisk) pelvic mass. The cystic component contains multiple irregular septations. (B) Ultrasound with Doppler shows internal vascularity of the solid component of the mass (white asterisk).**

and increased clear-white vaginal discharge since birth. She has noticed breast buds and darkening areolas. In clinic, patient's vital signs are unremarkable. Patient is >99 percentile in weight-for-age, >99 percentile in length-for-age, and 97 percentiles in BMI-for-age. Patient's physical exam was remarkable for tanner stage II breast buds, hyperpigmentation of the areolas, axillary hair, tanner stage III pubic hair, hyperpigmented labia without clitoromegaly, significant white vaginal discharge, acne on face and cheeks, and hair on arms and legs.

Laboratory values were significant for elevated estradiol at 668 pg/mL (normal  $\leq 25$  pg/mL), elevated estrone at 36 pg/mL (normal  $<15$  pg/mL), elevated testosterone at 90.51 ng/dL (normal 1.2–62.0 ng/dL), and elevated lactate dehydrogenase at 1107.0 U/L (normal 163–452 U/L).

Patient was referred from endocrinology clinic for a transabdominal pelvic ultrasound. Imaging revealed a heterogeneous cystic and solid adnexal mass measuring  $9.0 \times 7.5 \times 5.5$  cm (Fig. 1). There was internal vascularity within the solid component. The right ovary was visualized, though the left ovary was not visualized. Additionally, there was a post-pubertal appearance of the uterus and thickened endometrium for age.

Subsequently, patient was admitted and underwent MRI which again revealed a large mixed cystic and solid lesion located within the right lower quadrant and measured  $9.4 \times 5.2 \times 8.0$  cm (transverse x anteroposterior x craniocaudal) (Fig. 2). The internal solid component enhanced and restricted diffusion. Again, the left ovary was not visualized, and



**Fig. 2 – Magnetic resonance imaging of abdomen and pelvis. (A) Coronal T2 HASTE image demonstrates a large right sided mixed cystic and solid pelvic mass (white arrows). Additionally noted, rightward deviation of patient's uterus (white asterisk), which is enlarged for age. (B) Axial T1 VIBE fat-sat pre-contrast and (C) Axial T1 VIBE fat-sat post-contrast demonstrates enhancement of internal solid component (white arrows) of the pelvic mass. Axial DWI (D) and ADC map (E) demonstrates restricted diffusion of the internal solid component (black asterisks).**

there was a post-pubertal appearance of the uterus which was deviated to the right.

During admission, the surgery team was consulted. A left oophorectomy with surgical staging and peritoneal washings was performed. Intra-operative findings revealed a large mixed solid and cystic lesion of the left ovary, which did not involve the left fallopian tube. The left ovary and mass were resected and the left fallopian tube was spared (Fig. 3). The right ovary appeared normal.

Histopathology of the left ovarian solid component was consistent with a juvenile granulosa cell tumor of the left ovary (Fig. 4). The cystic component histologically demonstrated edematous ovarian tissue. Peritoneal washings were negative for malignant cells.

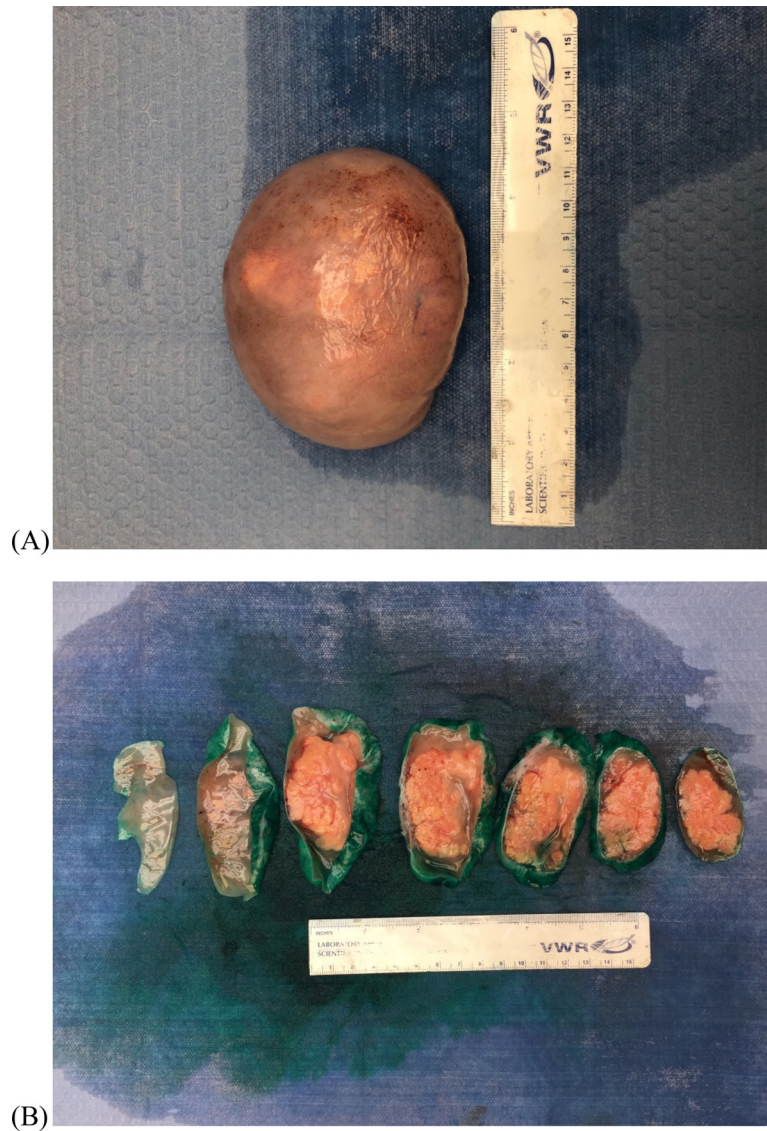
## Discussion

Granulosa cell tumors (GCT) can be characterized into 2 histologic categories: adult granulosa cell tumor and juvenile gran-

ulosa cell tumor. Adult GCT are much more common than juvenile GCT [1]. Ovarian tumors account for approximately 1% of all tumors in children and adolescents [2]. Juvenile granulosa cell tumors account for approximately 3%-7% of ovarian neoplasms [3,4]. Juvenile GCT are a rare type of ovarian sex-cord tumors. Other tumors in this class include thecoma-fibromas, Sertoli cell tumors, sex cord tumors with annular tubules, and gynandroblastomas [5]. Clinical significance is due to its estrogen secreting properties, resulting in “pseudoprecocity,” since ovulation does not occur [1]. Approximately 82% of pre-pubertal patients present with symptoms of precocious puberty including increased pubic hair, vaginal bleeding, breast enlargement and advanced bone age [3,5,6]. In addition to precocious puberty, abdominal mass can be another presentation [7].

Sonographically, granulosa cell tumors are usually solid and cystic or mainly solid with a spongiform appearance, with the solid portion being heterogeneous in echogenicity [8]. Cross-sectional imaging features can range from macroscopically solid masses to unilocular cystic struc-

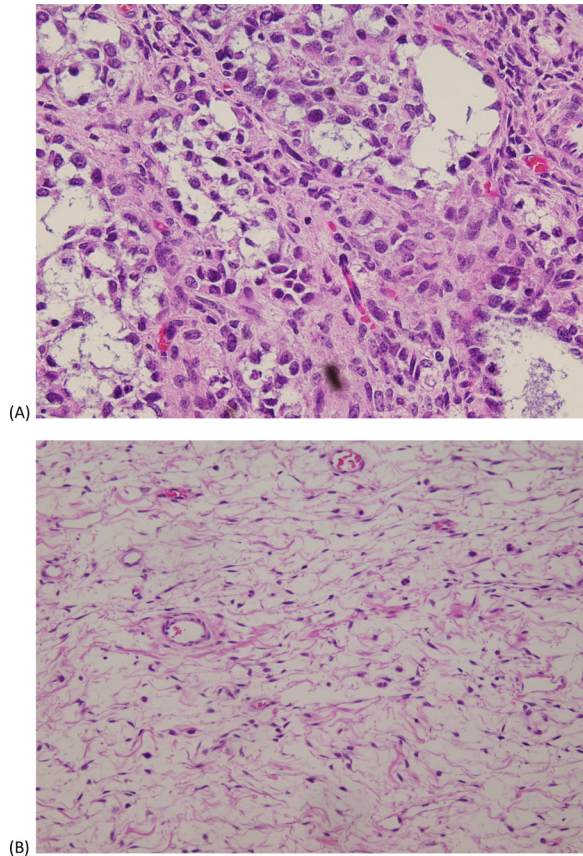




**Fig. 3 – Gross specimen before (A) and after (B) inking and sectioning.**

tures, but most often present as a mixed cystic and solid tumor [12]. Septations can appear thin or thick and irregular. On MRI, the solid component is typically isointense and enhances. There may be fluid-fluid levels within the cystic component, representing hemorrhage [1,9]. While imaging findings can be nonspecific and difficult to distinguish from other ovarian neoplasms, granulosa cell tumors rarely calcify or spread to the peritoneum, unlike epithelial neoplasms [1]. Additionally, uterine enlargement and endometrial thickening can be seen related to hormone secretion. Juvenile GCT are typically unilateral and confined to the ovary at diagnosis [3]. Greater than 90% are FIGO stage I at diagnosis [12]. Clinically, patients who have stage I disease respond well to unilateral salpingo-oophorectomy [4,6,7].

Interestingly in our reported case, the multilocular cystic component histologically revealed edematous ovarian tissue rather than cystic tumor component. While juvenile granulosa cell tumors have been associated with ovarian torsion [10], the lack of abdominal pain and/or tenderness and Doppler flow to the internal solid portion in this patient decreases the likelihood of this diagnosis in this case. Our hypothesis is that the estrogen effects stimulated the ovaries, similar to the hormonal effects of ovarian hyperstimulation syndrome (OHSS) and hyperreactio luteinalis (HL). Microscopically, both OHSS, and HL appear similar demonstrating marked edema of the luteinized theca layer and intervening stroma, as in this case [11]. Therefore, estrogen effects in this patient are hypothesized to cause the multicystic appearance radiographically and edematous ovarian appearance histologically (Figs. 1–4).



**Fig. 4 – Microscopic slides demonstrating predominantly solid appearing mass within the ovary (A) with gelatinous rim of ovarian tissue (B).**

### Conclusion

In summary, juvenile GCT are rare ovarian tumors found in children. Premenarchal children with juvenile GCT often present with precocious puberty due to estrogen-secreting properties of the tumor. Imaging characteristics can vary and are nonspecific but included mixed cystic and solid tumor, with an enhancing solid component. Prognosis is generally favorable as the majority of juvenile GCT are stage I disease

at diagnosis and patients typically respond well to unilateral salpingo-oophorectomy.

### Patient consent

Formal consent is not required for this case report with the use of entirely anonymized images from which the individual cannot be identified, and are not accompanied by text that might identify the individual concerned. Therefore, consent was not obtained for this case report.

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