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Case report

Coincidence of juvenile granulosa cell tumor and serous cystadenoma in a pediatric patient: Case report and literature review ☆,☆☆

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ABSTRACT

Juvenile granulosa cell tumor (GCT) is a rare ovarian tumor in children, presenting with a multiloculated cystic pattern and irregular wall-thickening on imaging and serous cystadenoma (SCA) is also another rare benign cystic ovarian tumor in children. The appearance of two uncommon types of ovarian tumors on both sides in children is extremely rare. We report the case of a 4-year-old female presenting with symptoms of precocious puberty and diagnosed with juvenile GCT on the left ovary after surgical resection. However, during follow-up 1 year after GCT resection, she presented with another multiloculated cystic mass in the right ovary, and diagnosed as SCA after surgical resection and histopathologic evaluations. The appearance of cystic ovarian tumor after primarily GCT resection need to differentiate between the recurrence of the primarily GCT and other cystic ovarian tumors although it is very uncommon. Furthermore, the imaging features played a key role in the differential diagnosis between benign and malignant ovarian tumors.

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Introduction

Ovarian granulosa cell tumor (GCT) is a rare sex cord-stromal tumor of the ovary, formed by cells thought to derive from those that surround the germinal cells in the ovarian follicles, accounting for only 2%–3% of all ovarian tumors [1,2]. Pathologically, ovarian GCTs can be classified into adult and juvenile forms, with juvenile types occupying 5% of all ovarian GCTs [2]. Ovarian GCTs typically have a favorable prognosis, with only a 25%–30% incidence of metastases or recurrences, categorizing GCTs as a low-malignant-potential ovarian tumor [3]. The radiological findings may indicate features of malignant ovarian masses, including wall irregularities, such as septal features and thickening; papillary projections; and solid, echogenic foci. The imaging characteristics of both adult and juvenile GCTs are nonspecific, and these tumors can be difficult to reliably distinguish from other ovarian neoplasms based on imaging features alone [4-7]. Due to superb soft-tissue resolution and the lack of radiation exposure, magnetic resonance imaging (MRI) is widely used as a problem-solving modality for the assessment of complex adnexal masses that are indeterminate on ultrasonography (US) or computed tomography (CT). Additionally, MRI can provide useful information for the accurate diagnosis of ovarian GCT [8]. Heterogeneous signal intensity (SI) on both T1-weighted imaging (T1WI) and T2-weighted imaging (T2WI) and high SI on diffusion-weighted imaging (DWI) are suggestive of an ovarian GCT diagnosis [9]. Ultimately, the final diagnosis requires histopathological analysis.

Epithelial neoplasms of the ovary account for 60% of all ovarian tumors and 40% of all benign tumors. Epithelial tumors comprise a small but significant proportion of pediatric ovarian masses [10]. Serous cystadenoma (SCA) is a benign serous tumor of the ovary, representing 16% of all ovarian epithelial neoplasms and accounting for two-thirds of benign ovarian epithelial tumors and the majority of serous ovarian tumors. SCAs commonly occur in adults of all ages, with reported mean ages ranging from 40 to 60 years, and rarely present in pediatric patients [11]. The imaging features of SCAs that suggest a benign cystic neoplasm include cyst unilocularity, minimal septations, thin walls, and the absence of papillary projections [12].

We present an extremely rare case in which a pediatric patient experienced both cystic GCT and SCA in the bilateral ovaries, which can result in misdiagnosis in clinical practice, affecting the treatment strategy and follow-up.

Case report

A 4-year-old female patient presented with increased breast size over a 6-week period. At the time of admission, anthropometric measurements were 22kg in weight (85 – 97th centile) and 116 cm in height (85 – 97th centile) according to the World Health Organization (WHO) growth chart [13]. A physical examination revealed a palpable mass in the left iliac fossa. A hormonal assessment indicated the elevation of serum estradiol levels to 133.2 pg/ml. An abdominal ultrasound revealed a large, multilobulated cystic mass with numerous septations of varying thickness, forming a sponge-like shape in the left iliac fossa (just above the uterus and bladder), suggesting an ovarian tumor (Fig. 1). The initial clinical diagnosis was precocious puberty due to an ovarian tumor.

On pelvic MRI, without contrast enhancement, a large, multilobulated, cystic mass was observed in the left pelvic region, containing multiple irregular septa that formed several compartments (resulting in a sponge-like or honeycomb-like shape), which contained homogeneous fluid-filled cysts. However, a small number of cysts appeared with blood-fluid levels, which presented high SI on T1W and T1-weighted fat saturation (T1WFS) imaging, indicating hemorrhage within the cysts. The largest diameter of this mass was approximately 101 mm. The mass compressed the bladder and forced the uterus to deviate to the right side. The left ovary was not identified, suggesting an ovarian origin for this mass. The right ovary and the uterus appeared normal in shape and SI. Additionally, a small amount of fluid collection in the Douglas pouch was observed, of approximately 5 mm. No evidence of abnormally enlarged lymph nodes was observed in the pelvic cavity (Fig. 2).

An exploratory laparotomy found a large ovarian cystic mass measuring 10 × 5 × 4 cm in size, with several small cysts observed in the area. Several cysts appeared to have ruptured, and a small amount of fluid was collected in the Douglas pouch. Several small pelvic lymph nodes and small ascites were negative for malignancy. Left salpingo-oophorectomy was performed, and this tumor was staged IC according to the International Federation of Gynecology and Obstetrics (FIGO) classification.

Histological sections of the specimen stained with hematoxylin and eosin (H&E) showed a tumor composed of numerous solid nets, clusters of cells with narrow cytoplasm and grooved, round-shaped hyperchromatic nuclei, and numerous small or microcysts containing eosinophilic secretions lined by some or numerous layers of cells, as described above (resembling Call-Exner bodies). Immunohistochemistry (IHC) analysis revealed positive reactions in the tumoral cells lining the cysts in response to antibodies for calretinin, inhibin, and Ki-67. These results were consistent with juvenile GCT (Fig. 3).

After the tumor was resected, the patient's serum estradiol level decreased to normal levels. She was continuously treated with adjuvant chemotherapy and routinely monitored. Unfortunately, after one year, imaging findings showed a new cystic mass in her right ovary on US and MRI (Fig. 4) while the estradiol level was normal (< 0.5 pg/ml). The images were unable to be distinguished from the potential recurrence of the initial GCT to other cystic ovarian tumors. The patient underwent tumor resection surgery after five months of the follow-up. Histologically, the post-operative specimen was compatible with SCA (Fig. 5).

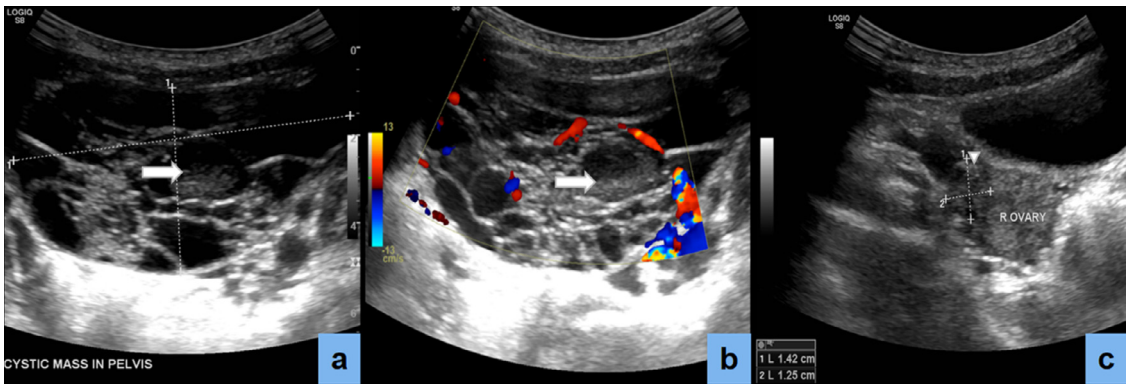

Fig. 1 – Abdominal ultrasound revealed a large, multilobulated, cystic mass of the left ovary, with numerous septations of varying thickness, forming a sponge-like shape (a). The lesion walls and septa appeared hypovascular on Doppler ultrasound (b). Several cysts presented fluid-fluid levels inside (arrows). The normal right ovary (arrowhead) was also observed on ultrasound (c).

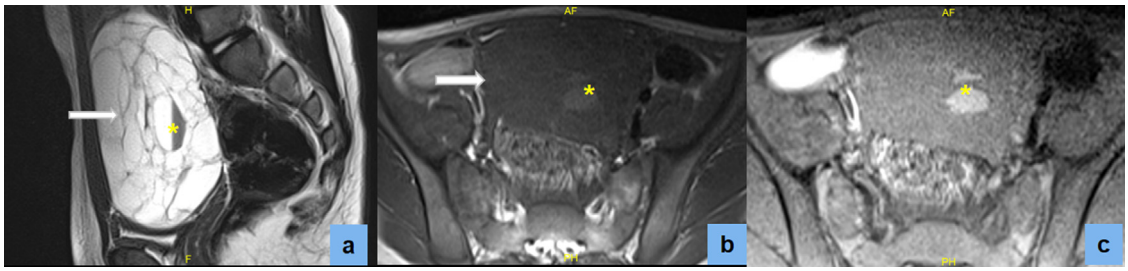

Fig. 2 – Pelvic magnetic resonance imaging (MRI) without contrast enhancement revealed a large, multilobulated cystic mass of the left ovary, featuring multiple, irregular septa forming many compartments (sponge-like or honeycomb-like shape), which contained homogeneous fluid-filled cysts (arrows) with hyper signal intensity (SI) on T2-weighted (T2W) imaging (a). A small number of cysts were observed with blood-fluid levels, low SI on T2W (a), high SI on T1-weighted (T1W) images (b) and T1-weighted fat saturation (T1WFS, c) images, indicating hemorrhaging within the cysts (asterisks).

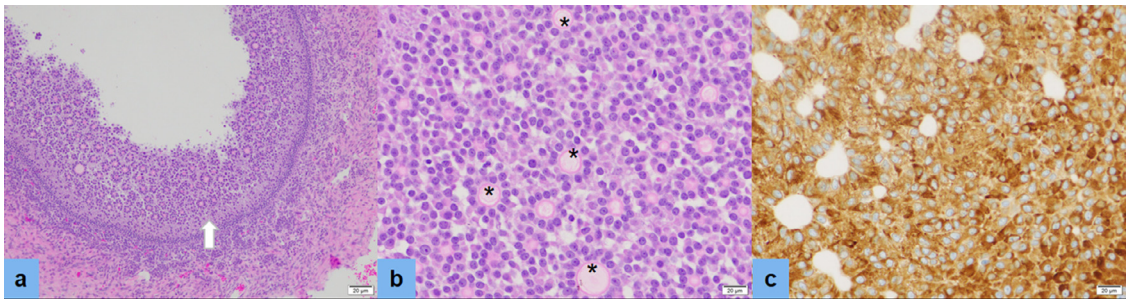

Fig. 3 – Microscopic examination (a: x 100 and b: x 400) of hematoxylin and eosin (H&E)-stained histological sections from the excised left ovarian tumor showed that the tumor was composed of numerous solid nets consisting of clusters of cells with narrow cytoplasm and grooved, round-shaped, hyperchromatic nuclei (arrow). Numerous small or microcysts containing eosinophilic secretions were lined with several layers of cells (asterisks). Immunohistochemistry revealed that the tumoral cells lining the cysts were positive for inhibin (c). These results are consistent with juvenile GCT.

Discussion

GCTs can be categorized into juvenile and adult types, reflecting the typical age of presentation, the differentiating histological characteristics, and differences in natural history [14,15]. Juvenile GCTs are rare, accounting for <5% of GCT cases, primarily presenting in prepubescent girls and women younger than 30 years [14]. Juvenile GCTs can be hormonally active, secreting estrogen. Therefore, most juvenile GCTs present with clinical evidence of precocious pseudo puberty, including breast development, pubic and axillary hairs, vagi-

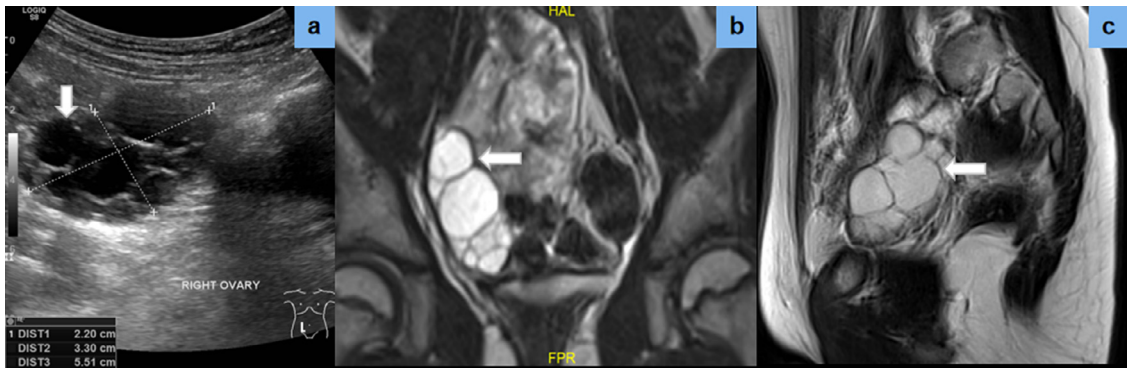

Fig. 4 – Abdominal ultrasound (a) showed a multilobulated cystic mass (arrow) of the right ovary, containing many regular septa. Similarly, the T2-weighted (T2W) coronal (b) and sagittal (c) magnetic resonance imaging (MRI) revealed a homogeneous cystic mass without a hemorrhage component, solid pattern, or papillary projection.

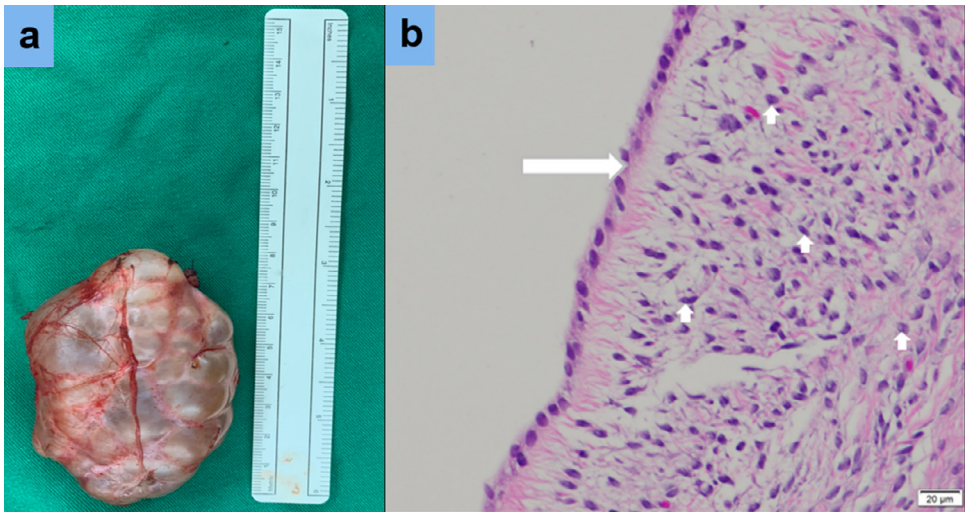

Fig. 5 – A macroscopic image on the excised right ovary (a) showed a multilobulated cystic mass with a smooth outer border and several small cysts inside. Microscopic (b: × 400) images of hematoxylin and eosin (H&E) histological sections showed that the cysts were lined with a single layer of tall, ciliated cells resembling normal tubal epithelia (long arrow). The cystic wall contained spindly fibroblasts several primordial follicles (short arrows). No evidence of malignancy was observed.

nal secretions, irregular uterine bleeding, and other secondary sexual characteristics [16]. In our case, the patient presented with increased breast size and growth beyond the threshold for age-predicted height and weight, indicating precocious puberty, and hormonal analysis confirmed that serum estradiol levels were elevated. These symptoms were consistent with existing literature reports.

The imaging findings for GCTs can vary widely, including solid masses, tumors with varying degrees of hemorrhagic or fibrotic changes, multiloculated cystic lesions, and completely cystic tumors. On cross-sectional CT and US imaging, GCT appearance can also vary widely but most often appears as a single, large, multiloculated cystic mass with solid components. GCT feature multiple septations, which can be thin or thick, and irregular. Intratumoral hemorrhage, central necrotic areas, and fibrous degeneration can result in a heterogeneous solid appearance [7]. GCTs do not present with calcifications or intracystic papillary projections, which are typical of epithelial neoplasms, such as serous or mucinous tumors. MRI tends to be more distinctive, with T1W images demonstrating high SI within the cyst, suggesting characteristic intratumoral hemorrhage in up to 71% of cases [4-7]. On T2W images, tumors present with a sponge-like appearance, indicating alternating solid and cystic spaces [8,9,14]. A sponge-like, multiloculated cystic mass filled with blood degradation products is a characteristic MRI sign of ovarian GCTs [2,17,18]. Kim et al. reported that hemorrhage in the tumor was a common MRI finding in a series of seven cases [19]. This feature may be useful for differentiating ovarian GCTs from other ovarian sex cord-stromal tumors.

Histologically, GCTs are categorized as a subtype of ovarian sex cord tumors. The ovarian follicles of juvenile GCTs are irregular in size and shape. The luteinization of juvenile-type tumor cells results in nuclei that are immature and show atypia and a high mitotic rate, in contrast with the adult type of GCT, which feature a low mitotic rate. Call-Exner bodies and

grooved, pale, round nuclei are classic features of the more common adult GST type, and the lack of these features can be used to distinguish the juvenile type from the adult type [15]. A positive immunohistochemical stain for inhibin, an ovarian glycoprotein, is a key diagnostic feature.

The FIGO staging system used for GCTs is the same system applied to other ovarian epithelial tumors. Tumor staging can be used to determine which patients are at risk for recurrence, which may require chemotherapy. Juvenile GCTs commonly occur at an early age and have an increased risk of recurrence compared with adult GCT [14]. Adult GCTs have precise clinical, histological, and evolutionary profiles [14,20]. Ovarian GCT generally has a favorable prognosis relative to other epithelial cancers. Primary surgery is the main treatment therapy for of GCT while role of adjuvant chemotherapy treatment remains debatable as no improvement in survival rates has been demonstrated. Therefore, chemotherapy is currently only recommended for patients with advanced, recurrent, or metastatic disease. Like other ovarian cancers, GCT can recur into the peritoneal cavity (unilateral side or bilateral side of pelvis) and the retroperitoneal space. In addition, there is a small amount of GCT occur on bilateral ovaries, approximately 2%. It is necessary to routine clinically follow up and analyse tumor marker (such as inhibin) in the detection of recurrent GCT after the initial diagnosis. As we mentioned above, GCT can secrete estrogen in some cases and it can be useful in monitoring tumor recurrence in some patients, but it is not sensitive enough to be used as a reliable tumor marker in this pathology [21].

Ovarian SCAs are a type of benign, ovarian epithelial tumor. On macroscopic findings, SCAs have a smooth outer surface and contain one or more thin-walled cysts filled with clear, watery fluid [11]. SCAs are typically unilocular by may be multiloculated. Microscopically, SCAs are composed of cysts and papillae, lined with non-stratified or stratified cuboidal to columnar cells and resembling the fallopian tube epithelium [11]. The immunohistochemical profile of SCA is similar to that of the normal ovarian surface and tubal epithelia. The most commonly used epithelial marker, p63, is positive in most SCA cases [22]. The symptoms and signs associated with large tumors tend to be nonspecific and commonly include pelvic pain, bloating, and discomfort [23]. Similar to many ovarian cystadenomas, tumor sizes range from 1 to 3 cm, are tumors typically represent incidental findings on ultrasound investigation. The SCA imaging features that are suggestive of benign cystic neoplasms include cystic unilocularity, minimal septations, thin walls, and the absence of papillary projections [12]. The combination of normal serum cancer antigen 125 (CA-125) assay results and imaging and clinical findings can be used to exclude the possibility of ovarian cancer. SCAs are benign lesions but can occasionally recur after incomplete resection. Although SCA is associated with better prognosis, they should also be assessed by an interprofessional team consisting of gynecologists, radiologists, and pathologists, to make ideal management decisions.

Two different tumors appearing on each ovary in pediatric patients is extremely rare, and we have not seen any reports in the literature. The appearance of a new multilobular cystic mass on the right ovary following a GCT resection of the left ovary can be confusing and recurrent GCT must be excluded, despite GCT being a tumor with low malignant potential. The US images and MRI revealed that the serous cystic tumor in the right ovary had a multilobed structure, with thin walls, and contained a homogeneous watery fluid, and no evidence of a hemorrhage component, solid pattern, or papillary projections. The histopathological images also revealed fluid-filled cysts lined by a thin layer of regular cells, which differed from the observed presentation of GCT, characterized by many layers of cells resulting in the irregular thickening of the inner walls and septa within the tumor.

Conclusion

Ovarian GCT is a rare tumor that arises from the sex cord-stromal tissue of the ovary, with low malignant potential, characterized by a variety of imaging features, among which a sponge-like, multilobulated cystic mass filled with blood degradation products is the most common presentation. SCA is a common benign ovarian tumor with an excellent prognosis that originates from epithelial cells, with typical imaging features indicating a cystic, thin-walled, fluid-filled tumor. Both of these tumors are rare in childhood, and the combination of these two types of tumors, each occurring in a different ovary, is extremely rare, and no previous mention of a similar situation was identified in the literature. SCA appearance after GCT resection could result in misdiagnosis as GCT recurrence. However, the typical benign characteristics of SCA observed on US and MRI can contribute to the differential diagnosis from a malignant ovarian tumor.

Ethical Statement

Appropriate written informed consent was obtained for the publication of this case report and accompanying images.

Author contributions

Le AV and Nguyen MD contributed to this article as co-first authors. All authors have read the manuscript and agree to the contents.

Patient Consent

Informed consent for patient information to be published in this article was obtained.

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