



Case report

Adult granulosa cell tumor with minor foci of juvenile granulosa cell tumor in postmenopausal woman: A rare case report

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ABSTRACT

Introduction: Granulosa cell tumor (GCT) is a rare neoplasm that is divided into adult GCT (AGCT) and juvenile GCT (JGCT). Generally, a patient will only have the AGCT or JGCT subtypes. Here, we presented the first case of AGCT accompanied by focal JGCT in a postmenopausal woman.

Presentation of case: A 63-year-old postmenopausal woman came with distended abdomen accompanied by postmenopausal bleeding. CT scan shows a solid mass with cystic degeneration. Laparotomy found a solid mass from the right ovary measuring 18 × 15 × 14 cm. The pathological results showed a diffuse tumor representing AGCT, accompanied by Call-Exner bodies and nuclear groove. In addition, minor foci were also found, which consist of well-defined margins tumor and follicular-like structures that resemble JGCT. The patient underwent bilateral salpingo-oophorectomy with a total hysterectomy and no recurrence in three months follow-up.

Discussion: Age and clinical symptoms cannot be used as specific differentiators between AGCT and JGCT. Radiological imaging also shows a similar appearance of solid masses tumors with hemorrhagic or fibrotic changes, multilocular cystic lesions, or completely cystic tumors. The concomitant findings of JGCT and AGCT could be distinguished very carefully by anatomical pathology examination. It is crucial to differentiate AGCT from JGCT, especially to see the prognosis.

Conclusion: The role of pathologists is needed in differentiating AGCT and JGCT, primarily when found simultaneously.

1. Introduction

Granulosa cell tumor (GCT) is a rare neoplasm that accounts for about 2–5% of all ovarian neoplasms [1]. GCT is divided into two types, namely adult GCT (AGCT) and juvenile (JGCT). AGCT is a low-malignant and late-recurrent ovarian tumor that is mainly reported in older women [2]. Meanwhile, JGCT is a rarer GCT mostly reported in prepubertal women and women under 30 years old [1]. Only 3% of JGCTs are reported in women over 30 years, and they are reported with a single microscopic appearance without the appearance of AGCT [3–6]. In this case, we present the first rare case of AGCT accompanied by focal JGCT in a postmenopausal woman. This study was approved by the

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2. Case presentation

A 63-year-old postmenopausal woman came with distended abdomen accompanied by postmenopausal bleeding for the past six months. There was no history of post-coital bleeding or pain. The patient had no history of tumors when he was young. A history of long-term drug consumption, tumors in the family, and smoking habits were also

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denied. On physical examination, the abdomen looks enlarged, soft, palpable solid mass at the level of the umbilicus. On rectovaginal examination, the solid mass has a smooth surface with good mobility. Ultrasound showed a retroflexed uterus measuring $7.9 \times 4.2 \times 5.3$ cm, homogeneous myometrium with a regular endometrial line 11.9 cm thick, and the left ovary with normal shape and size (Fig. 1A). The right ovary appears to be transformed into a solid mass with the regular outer surface, increased vascularity, color score 3, with an acoustic shadow image, the overall size of the tumor mass is $10.4 \times 12.9 \times 13.5$ cm, according to the picture of a solid ovarian neoplasm, possibly a GCT (Fig. 1B). At that time, the patient was planned for office hysteroscopy then exploratory laparotomy for frozen section. Laboratory examination results were within normal limits with tumor marker beta HCG value < 1.2 U/mL; AFP: 6.51 ng/mL; CA125: 186.3 U/mL; LDH: 185 U/L.

The patient then underwent a whole abdomen CT scan (Fig. 2A–D). A solid mass with cystic degeneration measuring $13 \times 18 \times 19$ cm appeared from the right adnexa with suspected GCT. No uterine, bladder, or rectal infiltration was seen. No lymph node enlargement is seen. Accumulation of fluid in the perihepatic, hepatorenal fossa, right paracolic, bilateral perivesical, and Douglas cavum.

Exploratory laparotomy found a solid mass from the right ovary measuring $18 \times 15 \times 14$ cm, smooth surface, and free of adhesions (Fig. 3A). After being cut, the inside was yellowish, and no papillary growths or cystic structures were found. There were no remarkable findings upon gross examination of the uterus, fallopian tubes, or left ovary. The above findings are in agreement with the FIGO staging 1C without surgical spill, capsule rupture, or malignant cells in ascites.

The frozen section results showed that the tumor tissue was arranged in a solid and diffuse pattern that matched the AGCT (Fig. 3B). Some of the tumor cells were relatively uniform with round nuclei. Slightly coarse chromatin, some with the nucleolus, eosinophilic cytoplasm, nuclear groove formations, and call Exner bodies, were seen (Fig. 3C). There were 1–2 mitosis/10 HPF with fibrovascular septa and thin-walled capillaries. The stroma is lightly inflamed with chronic inflammatory cells. In addition to AGCT, the typical features of JGCT were also found in the form of minor foci. The foci consist of a proliferation of granulosa cells that appear solid with well-defined margins and many cystic cavities between them (Fig. 3D). This cystic cavity is a follicular-like structure of varying size and shape lined with a layer of cuboidal to columnar cells with a hobnail nuclear appearance. The lumen is partially filled with a thin eosinophilic secretion. Tumor cells are round, small,

relatively uniform, with some deep-stained nuclei (Fig. 3E). Some tumor cell nuclei are spindle-shaped. The cytoplasm is abundant, eosinophilic some amphophilic. In the local swollen area found infiltration of cell debris and macrophage cells. To confirm this finding, we also consulted with two expert gynecopathologists and both of them shared the same opinion.

The patient was decided to undergo bilateral salpingo-oophorectomy and total hysterectomy. The patient was then treated for three days and returned home with a stable clinical condition, good mobilization, dry wounds, spontaneous defecation, and urination. The patient had no post-surgical complications, and there was no evidence of recurrence or metastasis during three months of follow-up.

3. Discussion

GCT is a rare neoplasm that accounts for about 2–5% of all ovarian neoplasms, usually differentiated into AGCT and JGCT [1]. Generally, a patient will only have the AGCT or JGCT subtypes. However, some rare cases, such as the study of Zhang et al. [5] and Young et al. [6] reported AGCT and JGCT feature simultaneously as the appearance of the JGCT is accompanied by minor foci of AGCT. Within our knowledge, our study is the first to report findings of an AGCT subtype with minor foci of JGCT in postmenopausal women. This section will discuss the characteristics of this case and its comparison with previous cases, both clinically, radiologically, and especially pathologically (Table 1).

Clinically, AGCT is more likely to occur in women aged 50–55, whereas JGCT occurs in younger women under 20 [8]. Because of this age difference, the symptoms experienced are also different. AGCT is usually typical with symptoms of postmenstrual bleeding, and JGCT is typical with symptoms of isosexual precocity [8]. This symptom of postmenstrual bleeding occurred in both this case and the case of Zhang et al. [5] Apart from being related to the patient's age, this symptom is a common endocrine manifestation that can also be accompanied by pelvic mass and pain. However, age and clinical symptoms cannot be used as specific differentiators.

Radiologically, our case showed a CT scan similar to a typical GCT, namely a solid right ovarian mass with central necrotic size and no peritoneal seeding [9]. However, radiological images also cannot differentiate AGCT from JGCT, let alone identify minor foci in this case. Although histologically, AGCT and JGCT have different features, these two subtypes have a similar gross appearance: solid masses tumors with

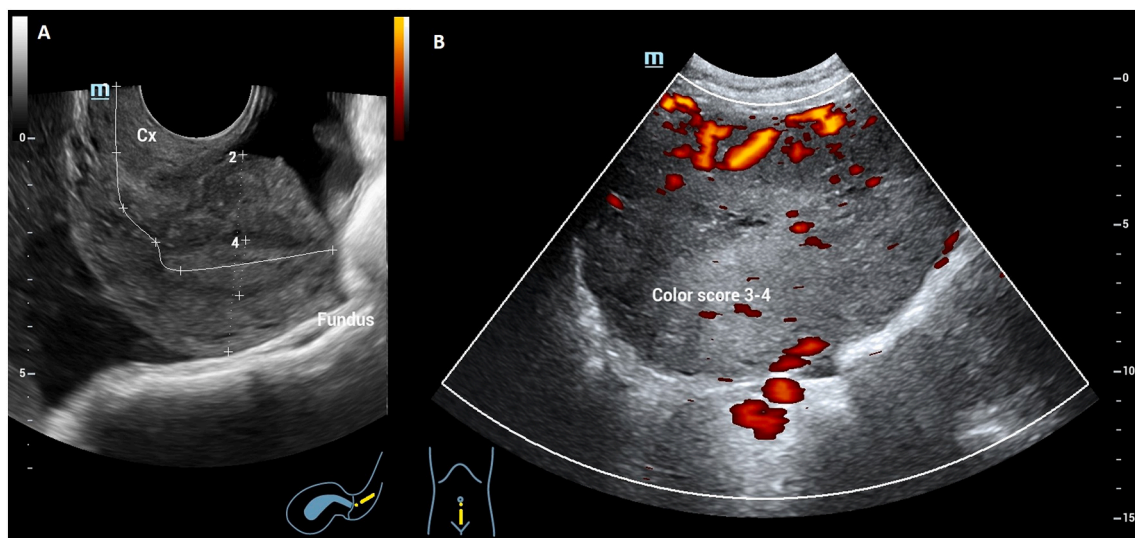


Fig. 1. Oncology ultrasound results showed (A) retroflexed uterus $7.9 \times 4.2 \times 5.3$ cm in size, 97.7 mL in volume, homogeneous myometrium with a regular endometrial line with a thickness of 11.9 mm. (B) Solid mass with a regular outer surface, increased vascularity color score 3, with an acoustic shadow, the overall size of the tumor mass is $10.4 \times 12.9 \times 13.5$ cm, volume is 966.7 mL possibly a granulosa cell tumor.

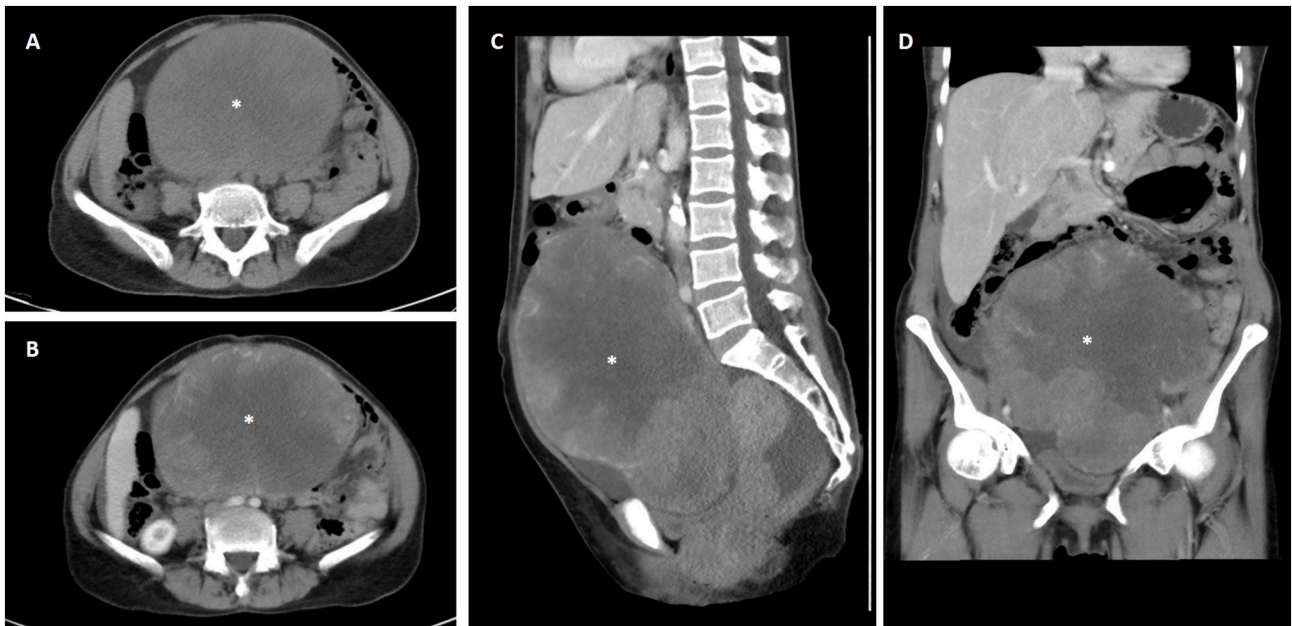


Fig. 2. Contrast-enhanced pelvic CT-scan (A) axial non-contrast, (B) axial contrast, (C) sagittal contrast, (D) coronal contrast showed a solid right ovarian mass (asterisk) with central necrotic size 13 × 18 × 19 cm. There is no sign of pelvic organ infiltration and small bowel infiltration. No sign of ascites and peritoneal or omental seeding.

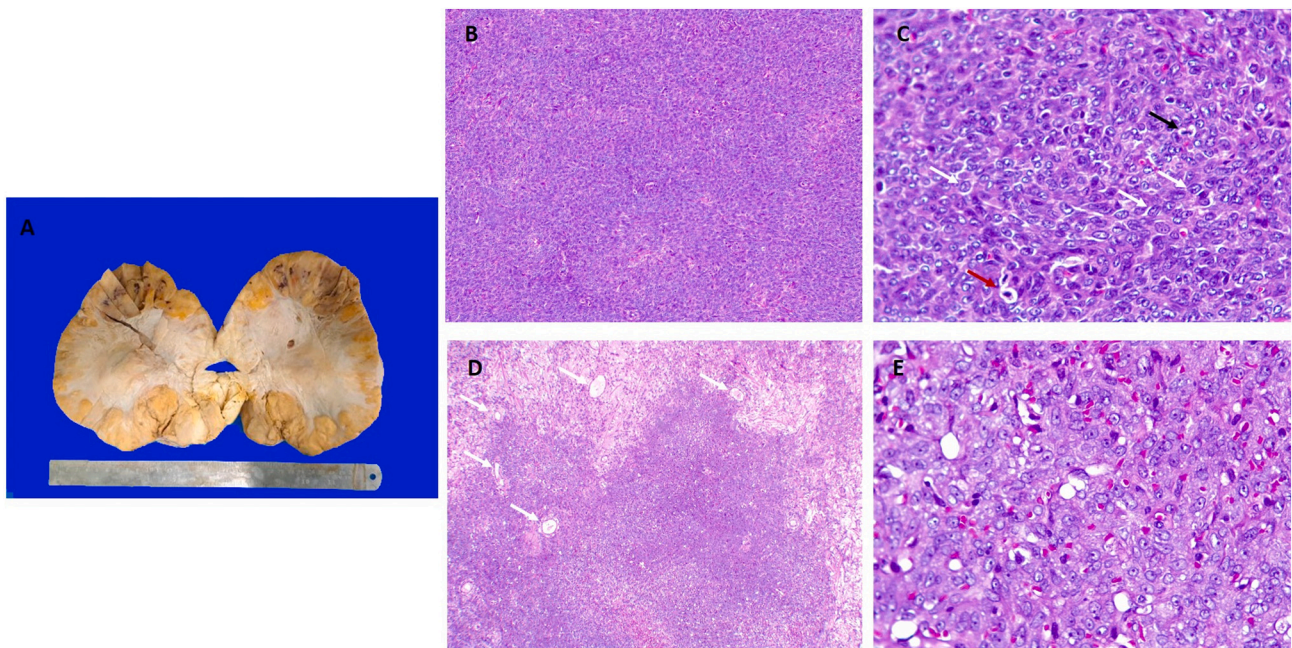


Fig. 3. On gross examination, (A) there was a solid mass from the right ovary measuring 18 × 15 × 14 cm, the surface was smooth and free of adhesions with a yellowish interior, and no papillary growths or cystic structures were found. On microscopic examination, it was found (B) AGCT with 100× magnification showing solid and diffuse tumor tissue; (C) AGCT with 400× magnification shows nuclear groove (white arrow), mitosis (black arrow), and Call Exner body (red arrow); (D) JGCT with 100× magnification shows solid tumor tissue with well-defined margin forming papillary with many follicular-like structures (white arrow); (E) JGCT with 400× magnification showed small round tumor cells with deep-stained nuclei and eosinophilic cytoplasm without a nuclear groove or Call-Exner body.

hemorrhagic or fibrotic changes, multilocular cystic lesions, or completely cystic tumors [3,9]. Therefore, it is not easy to distinguish these two subtypes only by radiological findings [3].

Because it is difficult to differentiate clinically and radiologically, the pathological role is crucial in determining AGCT or JGCT. In this case, AGCT is mainly seen from the diffuse histological pattern accompanied by the typical morphology of AGCT in the form of Call-Exner bodies and nuclear grooves. Meanwhile, in the minor foci of JGCT, there are tumors

with well-defined margins that form papillary with many follicular-like structures containing thin eosinophilic secretions that are not accompanied by Call-Exner bodies or nuclear grooves. In this case, the JGCT appearance in the minor foci is similar to the three main characteristics to diagnose JGCT, namely diffuse tumor cell growth with follicular-like structures, absence of Call-Exner bodies, and the characteristics of small tumor cells, round nucleus, deep chromatin, without nuclear grooves [5].

Table 1
Clinicopathological differences of AGCT, JGCT, and current case.

Characteristics	AGCT	AGCT with JGCT minor foci (current case)	JGCT with AGCT minor foci	JGCT
Clinical				
Age	50–55	63	53	0–20
Clinical symptoms	Perimenopausal/postmenopausal bleeding Pelvic mass	Postmenopausal bleeding Distended abdomen	Postmenopausal bleeding	Isosexual precocity Pelvic mass
FIGO staging	Vary	1C	1C	Vary
Radiological				
CT-scan	Solid masses Tumors with hemorrhagic or fibrotic changes Multilocular cystic lesions Completely cystic tumors	Solid right ovarian mass with central necrotic size	Not performed	Large, unilateral, multicystic mass with a solid portion and sometimes with irregular septa
Peritoneal or omental seeding	May present	Absent	Not performed	May present
Pathological				
Macroscopic	Vary	Maximum diameter 18 cm, encapsulated, smooth surface	Maximum diameter 20 cm, encapsulated	Vary
Microscopic				
Histological pattern	Microfollicular/macrofollicular Water-silk Gyriform Diffuse	Diffuse histological pattern, minor foci show tumor with well-defined margin forming papillary with many follicular-like structures containing thin eosinophilic secretion	Irregular follicular-like structure with internal mucin, minor foci show a diffuse histological pattern	Diffuse or macrofollicular Eosinophilic mucin Vacuolated cytoplasm Pseudopapillary pattern
Mitosis	Rare	1–2/10 HPF	>5/10 HPF	Frequent
Atypia	Minimal	Present, some with spindle-shape nuclei	Present	Present
Call-Exner Body	Common	Present, but absent in minor foci	Absent	Rare
Luteinization	Rare	Present in minor foci	Present	Common
Nuclear groove	Present	Present, but absent in minor foci	Present in minor foci	Absent
Surgical approach	Salpingo-oophorectomy Total hysterectomy	Bilateral salpingo-oophorectomy and total hysterectomy	Bilateral salpingo-oophorectomy and total hysterectomy	Salpingo-oophorectomy Total hysterectomy
Prognosis	Vary depending on FIGO stage and complete excision of the tumor	No recurrence in 3 months follow-up	First visit, loss of follow-up	Vary depending on FIGO stage and complete excision of the tumor

AGCT: adult granulosa cell tumor; CT: computed tomography; FIGO: The International Federation of Gynecology and Obstetrics; HPF: high power field; JGCT: juvenile granulosa cell tumor.

In this case, the concomitant findings of JGCT and AGCT certainly need to be distinguished very carefully. This is mainly because finding a follicular-like structure is not unique to JGCT because a small part of AGCT also has this structure. In addition, although Call-Exner bodies are significant markers for AGCT, 60% of AGCT may also lack this structure [10]. Therefore, we believe that in the absence of Call-Exner bodies, the differentiation of JGCT and AGCT should take full account of the nuclear characteristics and characteristics atypical of JGCT, which is small round and deep-stained nuclei. In addition, the small and irregular follicle-like structure in JGCT can also be used as a distinguishing characteristic [5]. It is crucial to differentiate AGCT from JGCT, especially to see the prognosis. JGCT is more likely to be interpreted as a malignant germ cell neoplasm that is AGCT [11].

In conclusion, AGCT with minor foci of JGCT patients has clinical and radiological conditions similar to GCT in general. Therefore, the role of an experienced pathologist is needed in differentiating AGCT and JGCT, primarily when found simultaneously. Nucleus and follicle-like structure characteristics in JGCT can be used as a differentiator, primarily when Call-Exner bodies are not found. More extensive studies are needed, especially to follow up the prognosis of AGCT with minor foci of JGCT patients.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Provenance and peer review

Not commissioned, externally peer-reviewed.

Ethical approval

This study was approved by the Institutional Review Board of Cipto Mangunkusumo National Hospital, Universitas Indonesia (IRB No. ETIK 21-08-0893).

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Declaration of competing interest

None.

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