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Case report

# Ruptured granulosa cell tumor of the ovary presenting with catastrophic intra-abdominal hemorrhage: A case report

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ABSTRACT

*Introduction and importance:* Adult granulosa cell tumor (GCT) is a rare stromal cell neoplasm that most often arises from the ovary. Presenting symptoms are related to external compression of adjacent structures (mass effect) or secretion of hormones such as estrogen. Patients most commonly present with irregular menstruation, postmenopausal bleeding, and abdominal pain. Prolonged estrogen exposure can contribute to endometrial adenocarcinoma development in untreated patients. The highly vascular nature of GCTs can lead to hemorrhagic rupture in rare cases.

*Presentation of case:* We describe a case of adult GCT in a 44-year-old female with a history of irregular menstrual bleeding and anemia. The patient presented with shortness of breath and abdominal pain. Computed tomography (CT) scan demonstrated possible hemorrhagic ascites of unclear etiology and a pelvic mass. The patient was brought to the operating room in hemorrhagic shock for surgical exploration where she was found to have active bleeding of a ruptured ovarian tumor for which she underwent left salpingo-oophorectomy. Postoperative course was unremarkable, and pathology demonstrated ruptured GCT.

*Clinical discussion:* Although rare, ovarian tumors can present with massive bleeding following rupture. Granulosa cell tumors are surreptitious as they grow slowly, and symptoms such as distention, abdominal pain, and irregular vaginal bleeding are nonspecific.

*Conclusion:* CT findings demonstrating a pelvic mass in the setting of spontaneous intra-abdominal bleeding should raise clinical suspicion, particularly in patients with histories of menstrual abnormalities. Patients with suspected intra-abdominal hemorrhage due to any cause are best treated by prompt surgical exploration and aggressive resuscitation.

## 1. Introduction

Granulosa cell tumors (GCTs) are rare sex cord-stromal cell tumors with a bimodal distribution of incidence due to juvenile and adult types [1,2]. Discussion of GCT here will be confined to the adult type. The incidence of GCT varies from 0.58 to 1.6/100,000 women per year [3]. Patients with GCT most often present with irregular vaginal bleeding, abdominal and pelvic pain, and distension [4,5]. Ultrasound is the imaging of choice to confirm clinical suspicion of a pelvic mass. Definitive diagnosis of a GCT is confirmed by histopathologic analysis following surgical removal, which is the mainstay of treatment [6,7].

Here we present a case of a ruptured GCT in a perimenopausal patient that presented as hemorrhagic shock.

SCARE criteria were followed during the preparation of this manuscript [8].

## 2. Case presentation

A 44-year-old woman presented to the emergency department with multiple syncopal episodes, dyspnea, and progressive non-radiating right flank and epigastric pain. She endorsed a 3-week history of non-bloody emesis and history of chronic irregular menstrual bleeding. Past medical history was significant for obesity, hypothyroidism, and anemia treated with blood transfusions. The patient denied allergies or use of home medications. Surgical history was positive for cholecystectomy and one Caesarean section. Family and psychosocial history

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were noncontributory.

On examination, the patient was hypotensive and dyspneic. The abdomen was soft, diffusely tender, and distended. A large, ill-defined, firm, and fixed abdominal mass was noted. Diagnostic laboratory testing exhibited a critically low hemoglobin of 4.9 g/dL, which was treated with transfusion of three units of packed red blood cells (PRBCs). Physical exam findings of abdominal mass, tenderness, and poor vitals prompted imaging to diagnose a possible surgical emergency such as gastrointestinal perforation or intra-abdominal bleeding. Non-contrast abdominal and pelvic computed tomography (CT) scan demonstrated a large pelvic mass with significant hemoperitoneum and possible capsular splenic rupture (Fig. 1). Massive intra-abdominal blood obscured the view of abdominal viscera making it difficult to identify the source of bleeding.

Due to rapid decompensation and failure to respond to resuscitation, emergent exploratory laparotomy was performed by the general surgery team. Intraoperative findings were notable for a large ruptured left ovarian mass with considerable hemoperitoneum, and the on-call obstetrician-gynecologist (OB-GYN) was called to the operating room. *En bloc* resection of the mass and left salpingo-oophorectomy was performed by the OB-GYN and general surgery team. A moderate amount of dark clotted blood was evacuated from the abdomen, and copious irrigation was performed. There was obvious tumor spillage noted during initial exploration. An additional resection of retroperitoneal tissue adjacent to the ovarian pedicle was performed to ensure the mass adhesions had not damaged surrounding structures and to achieve adequate margins. The remaining exploration of the abdomen and pelvis was unremarkable, including the spleen. During the procedure, the patient received two units of PRBCs, two units of fresh frozen plasma, and one unit of platelets. Estimated blood loss was 2000 $cm^3$. Postoperative hemoglobin was 9.7 g/dL.

The patient was transferred to the intensive care unit where she arrived intubated and sedated and continued to receive aggressive blood pressure support, one unit of platelets, and one unit of PRBCs. The patient was anuric, producing less than 90 $cm^3$ of urine on postoperative day (POD) 1 with a serum creatinine of 3.87 mg/dL. Urine output increased substantially on POD 2 to 800 $cm^3$. On POD 3, the patient was extubated, and norepinephrine was discontinued as hypotension subsided. Blood pressure was sustained with fluid resuscitation. The remainder of postoperative recovery was uneventful, and the patient was discharged on POD 9. A CT scan was completed one month after discharge showing complete resolution of the mass without recurrence or lymphadenopathy. The patient was referred to oncology for long-term follow-up to monitor for GCT recurrence every three months with pelvic examinations and serum tumor marker measurements. Chemotherapy was not initiated.

The excised, ruptured mass weighed 1969 g and consisted of two specimens, the larger measuring 19 × 18 × 6 cm and the smaller 10 × 4 × 2 cm. The inner aspect of the mass consisted of a tan to yellow solid, soft and not firm substance with interspersed areas of clotted blood admixed. None of the tumor material was noted to be on the capsular surface.

Microscopically, the tumor was highly cellular and predominantly in a solid configuration with some minor regions demonstrating an insular pattern. The nuclei of the tumor cells were monomorphous, being round to oval and angulated with fine chromatin and small but readily evident nucleoli (Fig. 2). Longitudinal nuclear grooves were noted in some but not the majority of the tumor cells. By immunohistochemistry, moderate cytoplasmic expression of inhibin was present in focal areas whereas a more extensive diffuse pattern of cytoplasmic staining was noted with calretinin (Fig. 3), confirming the pathologic diagnosis of adult GCT of the left ovary.

## 3. Discussion

Granulosa cell tumors are sex cord-stromal cell tumors derived from granulosa cells that account for only 2–5 % of ovarian tumors [1,9]. Adult GCTs present during the postmenopausal period with a median age of 50–55 years [9]. These indolent tumors generally grow slowly and present with nonspecific symptoms, allowing them to go unnoticed for years. Symptoms are related to mass effect and excess estradiol exposure. The most common initial manifestations of ovarian GCT are abnormal vaginal bleeding, pain, and distension [4,5,10]. Prolonged exposure of endometrium to tumor-derived estradiol may result in

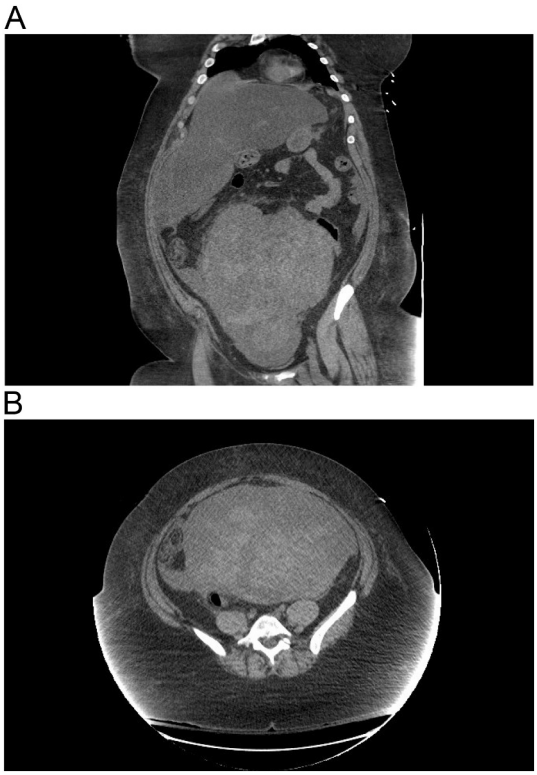


**Fig. 1.** (A) Frontal CT scan of patient. Hyperdense pelvic mass extending into the abdomen with diffuse hemoperitoneum. (B) Transverse pelvic CT scan of patient. Large hyperdense midline structure.

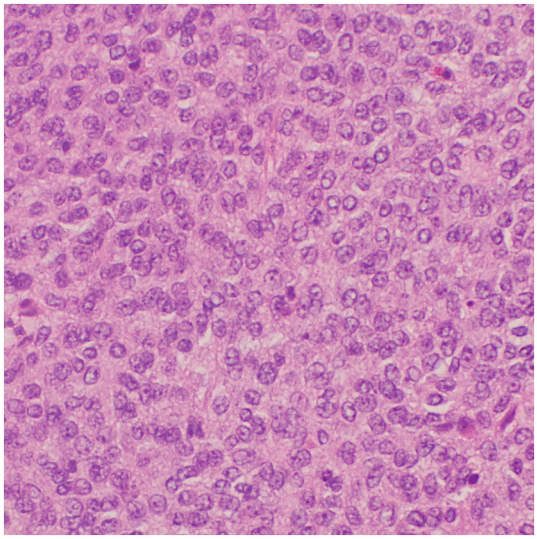

**Fig. 2.** Adult granulosa cell tumor with solid growth pattern consisting of tumor cells with oval to angulated nuclei, small nucleoli and inconspicuous cytoplasm (hematoxylin and eosin, 20×).

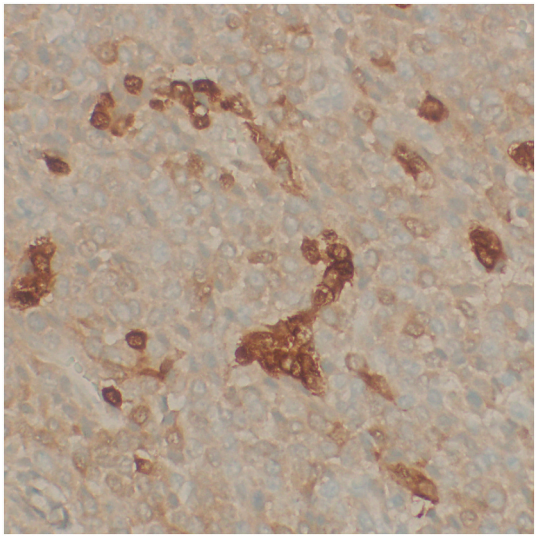

**Fig. 3.** Immunohistochemistry directed to calretinin (20×).

endometrial hyperplasia or endometrial adenocarcinoma in untreated patients [10]. Ultrasound is most often used to confirm the physical exam findings and to measure the mass. CT imaging is useful for evaluation of suspected GCT, particularly in the acute setting. Definitive diagnosis is confirmed by biopsy and histopathologic analysis after surgical removal.

This case describes a spontaneously ruptured ovarian GCT and acute life-threatening bleeding requiring aggressive resuscitation and prompt surgical exploration in a perimenopausal patient. Within the existing literature, the average GCT size is 12 cm, and the incidence of hemorrhage is less than 10 % [2,11]. Granulosa cell tumors grow to be highly vascular, making them prone to hemorrhagic rupture [3]. Patient presentation of a hemorrhagic GCT is nonspecific and does not always present as hemorrhagic shock [11–13]. The differential diagnosis for spontaneous intra-abdominal bleeding includes splenic rupture, ruptured ovarian cysts, ectopic pregnancy, ruptured abdominal aorta aneurysms and visceral artery aneurysms, and pancreatitis. Due to the lack of specificity in clinical symptoms, it is difficult to arrive at a definitive diagnosis prior to surgery.

The patient presented here was particularly difficult to evaluate due to body habitus. Obesity interferes with ultrasound assessment, making it difficult to obtain clear visualization of underlying organs. The patient's history of irregular menstrual cycles and bleeding may have been assumed to be secondary to obesity and hormonal imbalance [14,15]. Unexplained history of bleeding abnormalities and abdominal pain should raise suspicion for an ovarian tumor.

Laparotomy with complete tumor removal and histopathologic confirmation of the diagnosis, along with standard surgical staging, is the recommended treatment [3]. Characteristic histology for GCT demonstrates nuclear grooves or nuclei with a “coffee bean appearance,” which can be observed in Fig. 2, as well as Call-Exner bodies. Calretinin, a proposed marker of GCT, is used in pathohistological identification (Fig. 3) [16]. Premenopausal women presenting in reproductive years with early-stage disease are managed with tumor resection and unilateral salpingo-oophorectomy to preserve fertility [6]. In post-menopausal women and those who have completed childbearing, a total abdominal hysterectomy and bilateral salpingo-oophorectomy are recommended [6,7].

Despite the slow growth and silent nature of these tumors, most patients are diagnosed at an early stage. The key prognostic factor is the stage of the tumor at the initial surgery [7]. Those with low-risk stage I GCT should be observed following surgery [10]. Patients with GCT greater than 10 cm, tumor rupture, poorly differentiated tumor, and high mitotic index are high-risk and should consider adjuvant chemotherapy to reduce the risk of recurrence [9,10,17]. Stage II-IV GCTs should be treated postoperatively with chemotherapy [18]. Adjuvant radiation therapy in all stages of GCT is controversial, and its use is most often palliative for diffuse intra-abdominal and metastatic disease [10]. There is no standard approach to recurrent GCTs; however, surgical removal may provide long-term disease control [10,19]. Life-long follow-up with tumor markers, such as inhibin B, and periodic CT scans is strongly recommended regardless of stage as GCTs have greater than 40 % recurrence rate and potential for late relapse [1,10,20]. Ten-year survival rate is 84–95 % for stage I tumors, 50–65 % for stage II, and 17–33 % for stages III and IV [4,7,9]. Early recognition and surgical removal of GCT is critical to avoid unnecessary morbidity and mortality.

## 4. Conclusion

Granulosa cell tumors can present with the acute onset of massive intra-abdominal bleeding and hemorrhagic shock. Imaging demonstrating intra-abdominal bleeding and a pelvic mass without trauma should raise clinical suspicion for GCT. Patients with suspected intra-abdominal hemorrhage due to any cause are best treated by aggressive resuscitation and prompt surgical exploration. Definitive diagnosis of GCT relies on histopathological studies after surgical removal, which is the mainstay of treatment.

## Informed 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 case report got ethical approval from our institution. The patient was given consent form before the surgery.

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## Research registration number

Not applicable.

## Credit authorship contribution statement

Alexa D. Smith provided substantial contributions to acquisition of data and drafted the article; Peter Muscarella, MD, Mojdeh S. Kappus, MD, Martin J. Caliendo, MD and Connor Foote revised the article critically for important intellectual content; Peter Muscarella, MD gave final approval of the version of the article to be published; Wilfrido D. Mojica, MD provided histopathological images and data; and all authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

## Declaration of competing interest

None declared.

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