Clinical Case Report

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A rare case report of ovarian juvenile granulosa cell tumor with massive ascites as the first sign, and review of literature

Case report and review of literature

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Abstract

Rationale: Massive ascites as the first sign of ovarian juvenile granulosa cell tumor (JGCT) in an adolescent is an extremely rare, and its clinical features and treatment methods have not been well described.

Patient concerns: The clinical characteristics, diagnosis, and treatment methods in a 19-year-old girl who presented with massive abdominal distention and ascites was retrospectively reviewed. Abdominopelvic ultrasonography showed a large amount of ascites. The nature of ascites was exudate. All tumor markers were normal, but ascites and serum tumor CA125 levels were significantly increased. Abdominal CT showed left attachment area teratoma and right attachment area capsule solid change.

Diagnoses: Histological and immunohistochemical results were compatible with JGCT. Based on the FIGO classification, the patient with only malignant ascites was categorized into stage IC.

Interventions: The patient underwent mass resection with salpingoophorectomy. Following the operation, she received 6 courses of adjuvant chemotherapy with Nedaplatin and Paclitaxel liposome.

Outcomes: The patient was followed up postoperatively for 6 months to date without recurrence.

Lessons: We should be highly vigilant the JGCT with massive ascites as the first clinical manifestation.

Abbreviations: CR = calretinin, FIGO = International Federation of Gynaecology and Obstetrics, JGCT = ovarian juvenile granulosa cell tumor, PB = peripheral blood, TP = adjuvant chemotherapy with Nedaplatin and Paclitaxel liposome.

Keywords: ascites, diagnosis, ovarian juvenile granulosa cell tumor, treatment

1. Introduction

Granulosa cell tumors (GCTs) is an extremely rare, sex cord-stroma tumors constituting only 1% to 2% of all ovarian malignancies.[1] On the basis of age of onset and clinicopathological characteristics, these tumors are subdivided into 2 distinct forms, the adult type (AGCT) and the juvenile type (JGCT), representing 95% and 5% of the tumors, respectively.[2] Compared with the adult type, which is more common in the fifth decade, JGCT is more rarely seen and the majority (90%) are reported in prepubertal individuals or those aged less than 30 years. As JGCTs are hormone-active ovarian tumors, common presenting symptoms include vaginal bleeding, pseudo puberty praecox, irregular menstruation, and rarely hirsutism or virilization or, secondary to steroid hormone production. Clinically, abdominal pain and abdominal distention are also common symptoms.[2–4] Although the majority of JGCT patients are easily diagnosed on the basis of these typical clinical symptoms at the an early stage disease (Stage I) and usually have a benign clinical course after simple excision (unilateral salpingo-oophorectomy), small proportion of patients diagnosed at the advanced disease (stage II-IV) usually have no typical clinical symptoms and clinical course with unfavorable outcome.[5] For example, the onset of severe ascites as the first sign in a patient with JGCT is an extremely rare and a standard treatment regimen is also lacking.

In this case report, we retrospectively studied clinical presentation, histopathologic and imaging features, and treat-

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Table 1

Laboratory observation upon admission.

Characteristics	Index	Normal range
Blood		
WBC, $\times 10^9$/L	4.81	4.0–10.0
RBC, $\times 10^{12}$/L	5.04	3.5–5.5
HB, g/L	149	120–155
PLT, $\times 10^9$/L	290	100–300
TP, g/L	69.4	60–82
ALB, g/L	45.6	35–55
AFP, ng/mL	3.1	0–8
CEA, ng/mL	1.3	0–5
CA199, U/mL	1.69	0–37
CA125, U/mL	601.1	0–35
β-hCG, mIU/mL	0.021	<3
HE, pmol/L	46.22	0–68.96
E2, pg/mL	60	20–40
FSH, mIU/mL	0.25	3.85–8.78
LH, mIU/mL	4.27	2.12–10.89
Anti-ANA	(-)	-
T-spot	(-)	-
Pleural fluid		
WBC, $\times 10^6$/L	44	-
RBC, $\times 10^6$/L	1000	-
TP, g/L	47.7	65–85
LDH, μ/L	274	313–618
ADA, μ/L	4.3	-
CRP, mg/L	13	-
CEA, ng/mL	2.69	-
CA125, U/mL	39.87	-

ADA = adenosine aminhydrolase, AFP = α-fetoprotein, ALB = albumin, CEA = carcino-embryonic antigen, β-HCG = human chorionic gonadotropin-β, CRP = C-reactive protein, E2 = estradiol, FSH = follicle-stimulating hormone, HE = human epididymis protein, LDH = lactate dehydrogenase, LH = luteinizing hormone, TP = total protein.

ment effects in a JGCT patient with severe ascites as the first sign, and reviewed patient outcomes described in published literature.

2. Case presentation

A 19-year-old girl presenting with a progressive painless abdominal distention for 1 week was recruited sequentially at the inpatient service of Department of Gastroenterology, the First People's Hospital of Changzhou, Third Affiliated Hospital of Suzhou University. Physical growth had been normal. Her menstruation was regular since 12 years of menarche. Before this, she had not experienced fever, vomiting, abdominal ache, or jaundice.

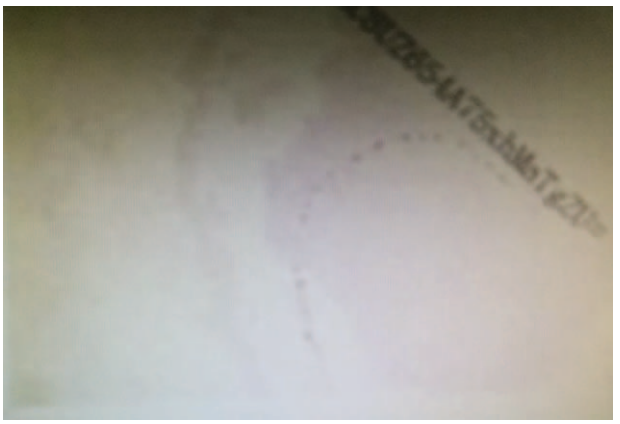

Figure 1. Cytology characteristics of ascites. Cytology characteristics of ascites were negative for malignancy.

Upon admission, a physical examination revealed shifting dullness on a very distended abdomen. She was found to have a remarkable level of serum and ascites CA125, while α-fetoprotein (AFP), carcino-embryonic antigen, CA199, CA153, and human chorionic gonadotropin-β in the patient were all within normal limits. However, as listed in Table 1, other laboratory data, including peripheral blood counts and sex hormones, were all unremarkable. In addition, cytology of ascitic fluid was negative for malignancy (Fig. 1).

Abdominopelvic ultrasonography revealed massive amounts of ascites and a cystic lesion with few septations in the pelvic cavity that measured 50 mm × 60 mm in greatest diameter. Abdominal contrast-enhanced computed tomography (CT) further displayed a well-marginated ovoid teratoma measured 50 mm × 40 mm in greatest diameter and seemed to have mostly arisen from the left adnexa. Right ovary was also enlarged with a solid cystic lesion of 50 × 50 mm in maximum diameter. Massive amounts of ascites in the abdominopelvic cavity were present (Fig. 2). Abdominal pelvic ultrasound and CT images did not show any evidence of gastrointestinal fistula, liquefactive necrosis, infiltration of other organs, or lymphadenopathy.

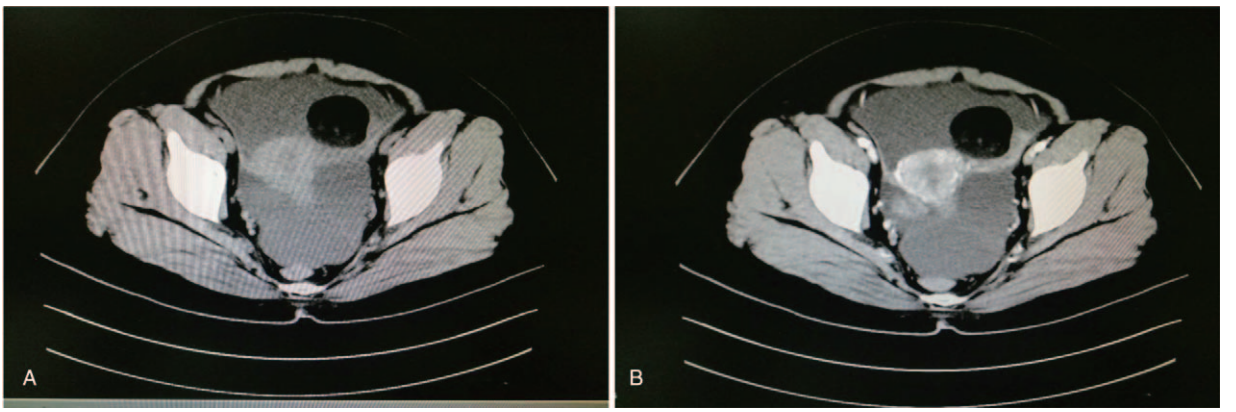

Figure 2. Conventional and enhanced CT images. Preoperative abdominal CT demonstrating a 50 × 40 mm left-sided solid ovarian teratoma with a smooth surface and a 50 × 50 mm right-sided solid cystic ovarian tumor with an irregular cauliflower surface as well as abdominopelvic ascites. (A) Conventional CT images; (B) Enhanced CT images.

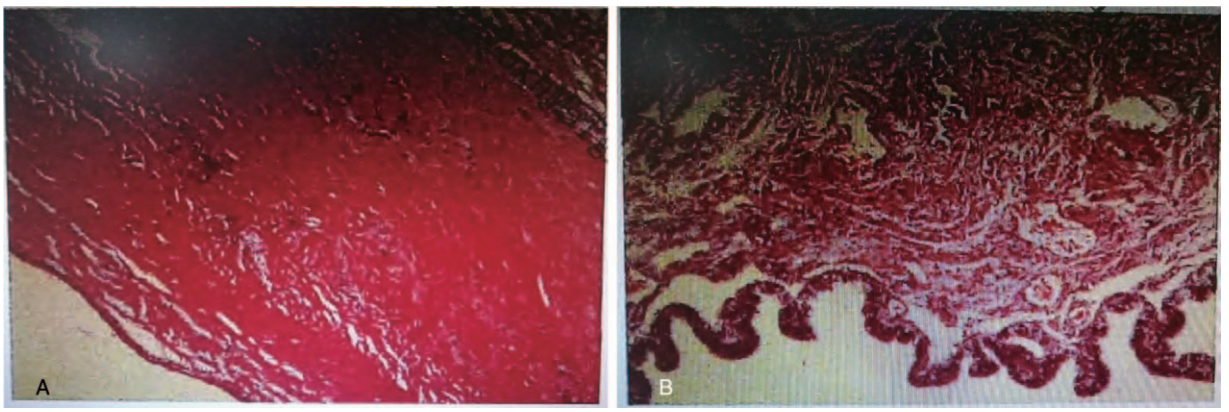

Figure 3. Histological examination. Histological section of (A) and (B) showing typical features of a juvenile granulosa cell tumor. The tumor cells have abundant cytoplasm; nuclei are large, hyperchromatic, and lack nuclear grooves. The cells are lining cystic follicles containing pale fluid. HE, ×400.

As the potential for ovarian malignancy could not be excluded, laparoscopic exploration was performed. At laparotomy, approximately 1200 mL of straw-colored, clear ascites was drained. Intraoperative displayed the left-sided solid ovarian teratoma with a smooth surface and the right-sided solid cystic ovarian tumor with an irregular cauliflower surface, and the capsule of the right-sided tumor was ruptured. In addition, the omentum and peritoneal surfaces presented several corn-like nodules. Retroperitoneal lymph nodes were not palpable. According to the patient's age and reproductive needs, a left oophorectomy and a right salpingo-oophorectomy were performed and biopsies from the omentum and peritoneum were obtained.

Frozen section was suggestive of ovarian sex cord stromal tumors. Further histologic examination revealed ovarian tissue partially replaced by a neoplasm of complex growth pattern with nodules of ovoid and polygonal pale eosinophilic to clear cells as well as multiple irregular follicles with cystic changes in some of them and proliferations of granulosa-like cells in the ovarian stroma associated with pseudopapillary projections compatible with JGCT (Fig. 3). Immunohistochemically, the tumor cells were positive for Inhibin-a, CD99, Vimention, Calretinin (CR), but were negative for AE1/AE3, EMA (-), SMA (-), Melan-A (-), CD10 (-). In the addition, Ki-67 proliferation index was quietly elevated in tumor (>5%).

On the basis of the histological features, and supported by the immunohistochemical findings, a diagnosis of JGCT was made. In order to analyze the tumor stage, the International Federation of Gynaecology and Obstetrics (FIGO) staging were used.[6] On the basis of the FIGO classification, the patients with only malignant ascites were categorized into stage IC. Therefore, following the operation, she received 6 courses of adjuvant chemotherapy with Nedaplatin and Paclitaxel liposome. The serum levels of CA-125 had dropped to the normal range and her ascites was in complete remission without any residual tumor in a 6-month follow-up period.

3. Ethic statement

Our institutional review board was waived due to the retrospective nature of the study. Informed consent was obtained from the patient's parents for the publication of this case report.

4. Discussion

JGCTs are rare and sexcord-stromal ovarian tumors constituting for the 5% to 8% of ovarian malign neoplasms. Only about 5% of GCT cases, which differ in their characteristic, histopathological features, and hormonal activities are of juvenile type, which is generally reported in prepubertal girls.[2–5] As JGCTs are hormonally active, the majority of patients had some of the typical features such as irregular vaginal bleeding, abdominal distension with pain, breast enlargement, development of pubic and axillary hair, vaginal secretions, and somatoskeletal changes.[7,8] However, the patient in our report did not have such typical symptoms, and her presentation was mainly massive ascites leading to the sudden enlargement of the abdomen. Furthermore, her ascites was gradually absorbed soon after the surgery. There is 1 similar reported case of fibroma with ascites and pleural effusion, which resolve after removal of the tumor.[9] However, to the best of our knowledge, massive ascites as the first sign of JGCT in an adolescent has not reported yet.

In general, there is no specific tumor marker of JGCT. Previous studies have shown that the measurement of serum β-hCG and AFP level was important to exclude secreting germ cell tumors,[10] which were normal in the present case. In addition, our case revealed a high level of serum and ascites CA125 that resolved dramatically after removal of tumor, without any recurrence, suggesting that CA125 level may be a tumor marker to assess for residual or recurrent for malignant epithelial ovarian tumor in a woman with massive ascites.[11]

Generally, most of patients with JGCTs are diagnosed in stage I level, with a tumor limited to the ovary, and usually have a benign clinical course after simple excision. A small proportion of children presented with advanced stages II-IV level are more difficult to treat and have a very poor prognosis.[12] Our case revealed a well-circumscribed, solid ovarian mass, and ascites by the diagnostic modalities for JGCTs, which include CT and ultrasonography scans. Although the morphological features that can be helpful in determining prognosis of JGCT were revealed, the golden standard method in JGCT diagnosis was histopathological evaluation. In our case, histopathology revealed granulose cells with nuclear atypia and common mitotic activities as well as foci Call–Exner bodies, which are a diagnostic marker for JGCT.[13] Further immunohistochemical evaluation showed positive for Inhibin-a and calretinin (CR), which are most helpful parameters in the diagnosis for JGCT.[14,15] CD99 is used

to be a marker preferred in differentiation of JGCT from low differentiated carcinomas of ovary, as it reacts with normal sertoli and granulosa cells.[16] Moreover, SMA and vimentin are also immunohistochemical markers confirming the diagnosis of JGCT.[17,18]

According to the FIGO, the primary management of JGCT is unilateral oophorectomy or salpingoophorectomy to preserve fertility in stage IA, IB, or IC of the child-bearing women. In treatment of advanced-stages JGCT (Stage II-IV), tumor and metastases should be extracted by cytoreductive surgery. In advanced stages of JGCT, prognosis is more worse, and after surgery, adjuvant chemotherapy is recommended for younger women with resected stage IC to IV GCT and appears to contribute to long-lasting remissions.[12,19] The patients are currently treated with platinum-based chemotherapy and reports on their effectiveness suggest an overall response rate of 63% to 80%.[20,21] In addition, related trials on platinum and taxane combination chemotherapy are also reported.[22] There is no evidence on the possible benefits of radiation or hormonal therapy for JGCT patients. In our case, left oophorectomy together with right salpingo-oophorectomy without lymph node dissection were performed for conserving the fertility of patient. As malignancy suspicion was shown in frozen sections, the patient received adjuvant chemotherapy with Nedaplatin and Paclitaxel liposome postoperatively, and in her 6 months follow-up, there was still no sign of metastasis or recurrence.

5. Conclusion

Advanced-stage JGCT presented with massive ascites, especially in young girls, should be considered in the differential diagnosis of aggressive ovarian JGCT tumors. In preoperative diagnosis, both the increased levels of serum estradiol and CA125 as well as the radiological evaluations should alert for JGCT. However, further accurate diagnosis only depends on histological and immunohistochemical investigations.

Author contributions

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Writing – review & editing: Liwen zhang.

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