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An Extremely Rare Torsion Case of Ovarian Yolk Sac Tumor in Postmenopausal Woman

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Abstract

An extremely rare case of ovarian yolk sac tumor (YST) with adnexal torsion in a postmenopausal woman is presented. A 66-year-old woman visited the emergency department of Gujo City Hospital with lower abdominal pain. Elevated serum AFP levels and preoperative imaging suggested torsion and possible dissemination of ovarian malignancy, and a semi-urgent debulking surgery for suspected ovarian cancer was performed. Histological and cytological examinations confirmed YST with omental dissemination. Immunohistochemistry showed positivity for SALL4 and loss of phosphatase and tensin homolog (PTEN). The final diagnosis was torsion of a pure-type YST originating from the left ovary, staged as pT3CN0M0. No BRCA mutations were detected; however, the genomic instability score was positive (44 > 42). Given the poor expected prognosis, the patient received adjuvant chemotherapy including both bleomycin, etoposide and cisplatin (for germ cell tumors) and paclitaxel, carboplatin, and bevacizumab (for epithelial ovarian carcinoma). Four months after surgery, the patient shows no evidence of recurrence or relapse.

Keywords

Yolk Sac Tumor, Postmenopausal, Torsion, Loss of PTEN

1. Introduction

Ovarian germ cell tumors (GCTs) account for approximately 15% to 20% of all ovarian tumors and 2% to 5% of all ovarian malignancies. Ovarian yolk sac tumors

(YSTs) account for 14% to 20% of all malignant ovarian GCTs [1]. The age distribution of YST patients has been reported to range from 16 months to 86 years of age, but two-thirds are under 20 years old, and it is sometimes seen in postmenopausal women [2]. Postmenopausal YST patients may have different characteristics and a less favorable prognosis compared to younger patients [3] [4].

In older women, malignant neoplasms with YST differentiation may rarely occur [5] [6]. Another component of GCT is mostly of GC origin, while the component of Müllerian-type cancer may be associated with somatically derived tumors. Some of the pure type YST may be of GC origin, while others may be of non-GC origin as these were not detected or somatic origin. Recently, pure YSTs in older adults have been reported to have originated from mutations similar to those found in pure YSTs in younger adults, while other pure YSTs exhibited molecular profiles similar to previously somatically derived YSTs, suggesting that somatically derived YSTs are associated with an undetected Mullerian carcinoma component rather than a GC origin [7]. In this case, PTEN and p53 immunohistochemical staining were added to search for the origin.

In this case, the patient presented to the emergency room with acute abdominal pain and was diagnosed with ovarian tumor torsion, for which treatment was initiated. Adnexal torsion occurs usually in women of the reproductive age and is often a benign ovarian tumor, although it can rarely occur in postmenopausal women. Ovarian malignancies rarely torsion due to invasion and adhesion to surrounding tissues, occurring in less than 2% of cases [8]-[10]. In the present case, a postmenopausal woman presented with severe pain in the lower abdomen. Preoperative imaging showed findings suggestive of torsion of the left ovarian tumor, and disseminated lesions were observed. All epithelial tumor markers were negative, but only AFP showed an abnormally high value, leading to a preoperative diagnosis of torsion of a YST with dissemination.

2. Case Report

A 66-year-old married woman with no history of pregnancy presented to the emergency department of Gujo City Hospital with lower abdominal pain that had persisted for 4 - 5 days. She had undergone menopause at the age of 50 and had received estrogen replacement therapy with an estradiol patch (0.72 mg every two days) and dydrogesterone (5 mg/day) intermittently from age 50 to 55. At age 35, she underwent an exploratory laparoscopy at another hospital for suspected endometriosis, but no abnormalities were identified. She was an HBV carrier due to vertical transmission. She had no other significant past medical or family history.

An emergency physician evaluated her, and a CT scan revealed a pelvic mass; she was referred to a gynecologist the same day. CT imaging suggested torsion, rupture, and hemorrhage of a left ovarian tumor, along with possible peritoneal dissemination (**Figure 1(a)**). MRI further indicated torsion, rupture and bleeding of a tumor consistent with an epithelial malignancy, YST, or GCT (**Figure 1(b)**, **Figure 1(c)**).

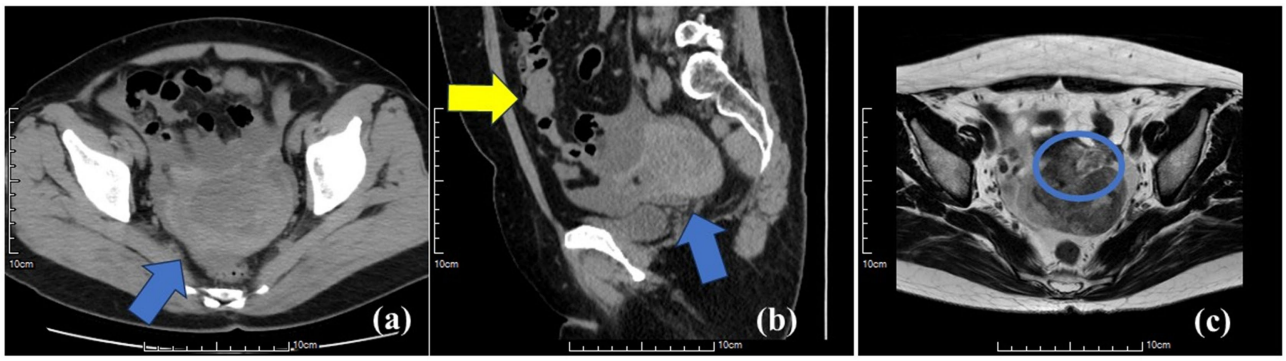

Figure 1. (a) Bloody ascites was observed in the pelvis. A mass with soft tissue attenuation was identified in the left ovary (blue arrow), surrounded by a faint hyperdense area suggestive of a hematoma; (b) The sagittal section also demonstrated findings suggestive of torsion (blue arrow). Multiple nodules with soft tissue attenuation were also observed in the peritoneal cavity (yellow arrow); (c) A multilocular cystic mass measuring 74 mm in diameter was observed. The mass showed a mixture of high- and low-signal intensity areas on T2-weighted imaging. A cord-like structure extending toward the center of the mass was identified, suggesting the twisted pedicle (blue circle).

Blood tests showed no abnormalities in CBC or CRP [WBC 6600 (4000 - 9000)/μl; CRP 0.02 (<0.30) mg/dl]. Epithelial tumor markers were within normal ranges [CA125 8.3 (<35.0) U/ml; CA19-9 6.8 (<37.0) U/ml; CA72-4 < 1.0 (<10.0) U/ml]. Among hormone levels and other tumor markers, only AFP was markedly elevated at 582.7 (<10.0) ng/ml. Other laboratory values were as follows: LH 16.96 mIU/ml; FSH 48.30 mIU/ml; estradiol <5.0 pg/ml; progesterone < 0.05 ng/ml; testosterone 0.16 ng/ml; hCG-β < 1.0 ng/ml; SCC 0.6 (<2.5) ng/ml; neuron-specific enolase 15.4 (<16.3) ng/ml.

Preoperative imaging studies suggested the possibility of epithelial malignant tumors or other ovarian GCT, but only AFP, a marker for YST, showed abnormally high levels, while epithelial tumor markers were not elevated at all. Therefore, YST was the most likely diagnosis based on the preoperative findings.

Her abdominal pain subsequently subsided. Based on the above findings, a preoperative diagnosis of torsion, rupture, bleeding, and omental dissemination of a YST was made. The surgery was planned for the malignant tumor, and preparations for autologous blood donation were also necessary. Semi-urgent radical surgery for suspected ovarian cancer was scheduled for six days after the initial emergency department visit.

At abdominal exploration, the left ovary appeared dark red and friable, and the adnexal pedicle was twisted twice in a counterclockwise direction together with the fallopian tube (**Figure 2**). Approximately 150 ml of bloody ascites was present, and intraoperative cytology was performed. Cytological examination of the ascites revealed cells suspicious for YST (**Figure 3**). Macroscopically, tumors were observed in the left and right ovaries and fallopian tubes, with dissemination to the omentum and rectal surface. These lesions were also confirmed pathologically, as will be mentioned later.

The bilateral adnexa and uterus were completely removed, a partial omentectomy was performed (**Figure 4**), and a pelvic lymph node biopsy was obtained. As many

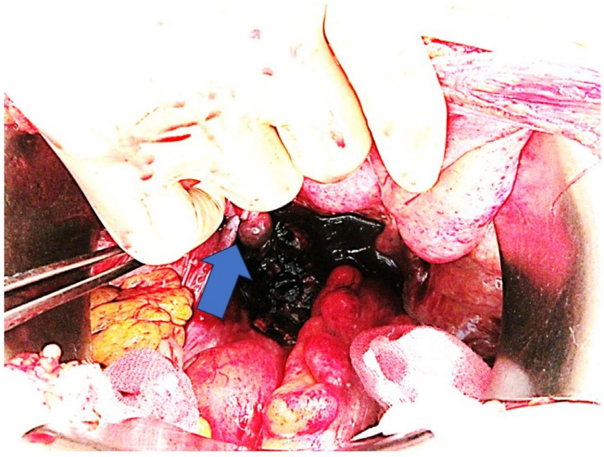

Figure 2. The left ovary appeared dark red and friable during surgery. The adnexal pedicle was twisted twice in a counterclockwise direction together with the fallopian tube (arrow).

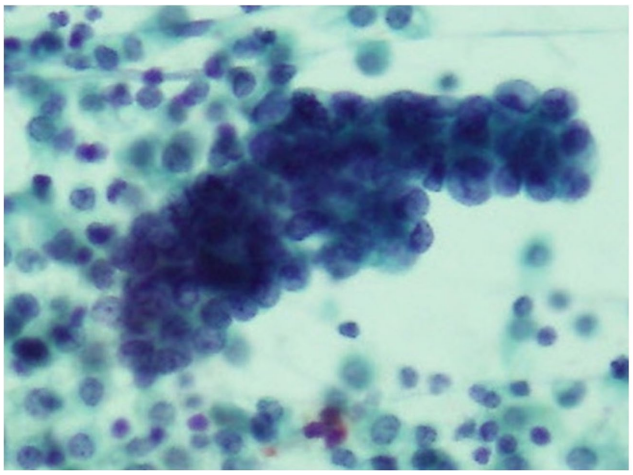

Figure 3. Highly atypical tumor cells formed overlapping clusters. In combination with the preoperative finding of markedly elevated AFP levels, a yolk sac tumor was suspected.

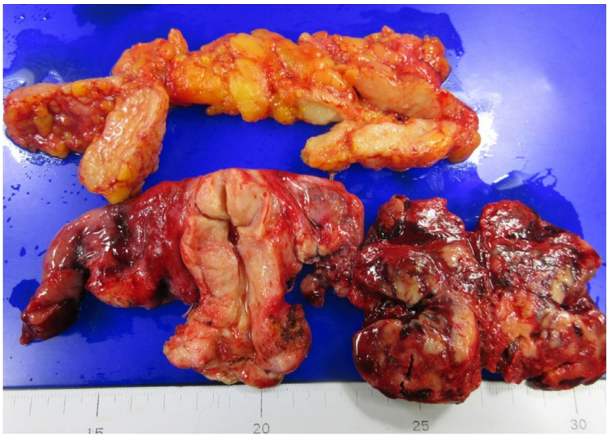

Figure 4. The removed specimen included the uterus, both ovaries, fallopian tubes, and greater omentum. The left ovary contained necrotic tissue and appeared dark red, while the cut surfaces of the tumorous portions of the left ovary and greater omentum were grayish-white.

disseminated lesions as possible were also resected. At the end of surgery, only superficial dissemination of approximately 1.5 cm on the rectal surface remained. A subcutaneous port for intraperitoneal administration of anticancer drugs was placed at the end of the procedure.

The left ovary showed marked hemorrhage and necrosis. The cut surface of the disseminated omental tumor was pale red, and intraoperative cytology demonstrated cells suspicious for YST, similar to those observed in the ascites. Macroscopically, the ovarian tumor was dark red with extensive hemorrhage, and multilocular cystic areas were also present (**Figure 4**). The patient's postoperative course was uneventful, and she was discharged on postoperative day 7.

Although macroscopically the tumor appeared to be the primary tumor, a detailed pathological examination was performed on the left ovary, which showed a strong tendency towards necrosis, and on the greater omentum, which had the largest dissemination and less tendency towards necrosis, specifically at the site of the largest cut surface. Pathologically, low-power examination of the left ovary revealed extensive hemorrhage and necrosis surrounding the tumor (**Figure 5(a)**). The highly atypical tumor cells exhibited a reticular growth pattern (**Figure 5(b)**). No epithelial malignancies or other GCT components were identified in any of the examined specimens. Immunohistochemical analysis demonstrated strong SALL4 expression in the tumor cells (**Figure 5(c)**) on all specimens, ruling out the presence of epithelial or Müllerian ductal components. This allowed for more appropriate confirmation of the diagnosis of pure YST. Additional staining for the tumor suppressor genes p53 and PTEN showed negative p53 expression and loss of PTEN in the tumor cells (**Figure 5(d)**).

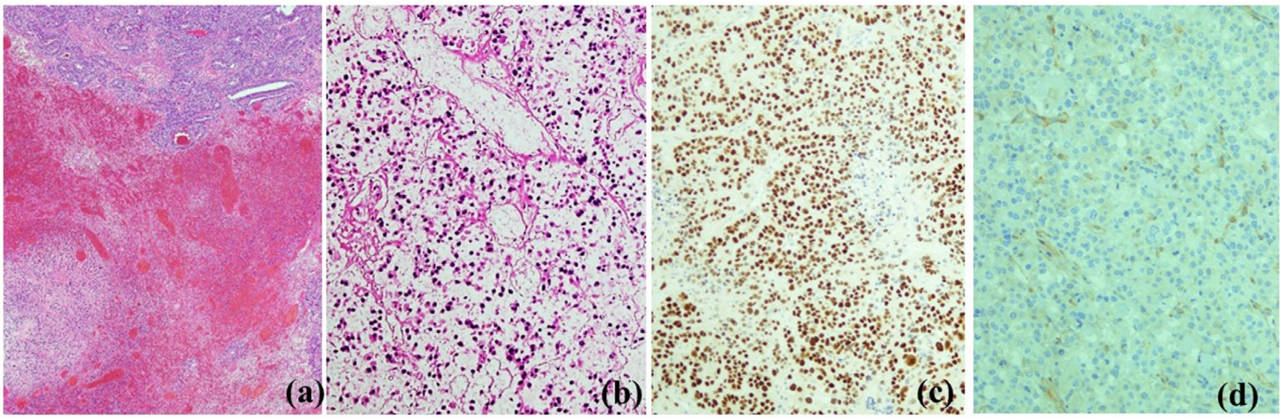

Figure 5. (a) Low-power view showing extensive hemorrhage and necrosis surrounding the tumor (H&E, 10×); (b) Highly atypical tumor cells exhibiting a reticular growth pattern (H&E, 20×); (c) Immunohistochemical staining demonstrating strong SALL4 expression in the tumor cells (sABC, 20×); (d) Immunohistochemical staining showing loss of PTEN expression in the tumor cells (sABC, 20×).

The final pathological diagnosis was torsion of a pure-type yolk sac tumor originating from the left ovary, staged as pT3CN0M0. This pure YST may share molecular characteristics with YSTs associated with endometrioid carcinoma, and since paclitaxel, carboplatin, and bevacizumab (PC-Bev) therapy for epithelial

malignancies was planned in addition to BEP therapy, maintenance therapy with a poly (ADP-ribose) polymerase inhibitor may be necessary [11], so BRCA testing and genomic instability scoring were performed. No BRCA mutations were detected; however, the genomic instability score was positive (44 > 42) according to the Myriad Genetics system®.

There have been reports that a complete cure is difficult with BEP therapy alone in elderly YST patients [12], so from the beginning, a total of 6 courses were planned: 2 - 3 courses of BEP therapy followed by 3 - 4 courses of PC-Bev therapy.

Regarding BEP therapy, the first course was administered as planned, but the second course was administered without bleomycin because pulmonary restrictive disorder, a possible side effect of bleomycin, was observed. Since pulmonary restrictive disorder can lead to pulmonary fibrosis [13], bleomycin was omitted from the second course, and BEP therapy was administered.

Following further consultation with the patient, the regimen was changed to PC-Bev from the third cycle onward. The plan was moved up, and PC-Bev therapy was started from the third course, with 3 more courses planned.

The AFP level, which had been markedly elevated preoperatively (587 ng/ml), decreased to 12.1 ng/ml one month after surgery. Four months have passed since the operation, and there are no signs of recurrence or relapse.

3. Discussion

Ovarian YSTs are typically diagnosed in childhood or adolescence and are extremely rare around or after menopause. Wang *et al.* reported that the average age of onset in postmenopausal women was 62.5 years (range, 48 - 96), which is consistent with the present case. In that study, AFP levels were not routinely measured preoperatively in postmenopausal patients, and only a small number of cases with preoperative AFP measurements showed values within the normal range [14]. In the present case, preoperative imaging findings combined with markedly elevated AFP levels—despite a normal CA125 level—strongly suggested ovarian YST with torsion and dissemination. Considering these findings together with the patient's acute abdominal pain, a preoperative diagnosis of torsion of a yolk sac tumor with dissemination was possible, even though the patient was postmenopausal.

Because of the small number of reported cases, the molecular characteristics of pure YSTs in older women—whether of germ cell (GC) or non-GC origin—remain poorly understood [15]-[18]. In a recent report by Numan *et al.*, targeted next-generation sequencing revealed that one pure YST harbored alterations in DICER1, PIK3R1, PTPRT, PMS1, and TP53, while another pure YST exhibited alterations in PTEN, ARID1A, ARID1B, FGFR2, and CTNNB1, which are commonly associated with endometrioid carcinoma. In contrast, somatically derived YSTs demonstrated shared mutations between both components, including TP53, KRAS, FBXW7, and KMT2C, suggesting a common origin [7]. These findings indicate that pure YSTs in older women may arise through at least two distinct pathways: a GC-derived pathway, showing molecular alterations similar to those seen

in pure YSTs of younger patients, and a somatic (Müllerian carcinoma–associated) pathway, in which tumors exhibit molecular profiles consistent with somatically derived YSTs and may contain unsampled Müllerian carcinoma components. In the present case, immunohistochemistry showed negative p53 staining but loss of PTEN expression, suggesting the possibility of PTEN alteration [19]. Based on limited immunohistochemical staining results, it is possible that this pure YST shares molecular characteristics with endometrioid carcinoma–associated YSTs, but not conclusive.

In general, ovarian GCTs are highly malignant, but they are considered curable with surgical treatment and combination chemotherapy. The BEP therapy is recommended as first-line chemotherapy, and the 5-year survival rate is close to 90%. Prognostic factors for ovarian YSTs have been reported to be tumor staging [20], ascites volume [21], serum AFP reduction rate [21], residual tumor [22], and chemotherapy regimen and number of treatments [22] [23]. The prognosis for ovarian YSTs in postmenopausal women is poor even in the early stages, with early recurrence and metastasis occurring even in stage I [4]. Thus, some reports suggest that ovarian YSTs in elderly patients, regardless of whether or not have an epithelial component, should be treated with BEP therapy with combination with the regimen for epithelial ovarian cancer, like as PC-Bev [12]. In this case, the possibility of pulmonary-restrictive disorder emerged after one course of BEP therapy. Due to the potential side effects of BLM, the second course of BEP therapy was administered without BLM, and from the third course onward, the therapy was changed to PC-Bev therapy.

SALL-like protein 4 (SALL4) is considered a useful marker for the histological identification of YST components and is more sensitive than AFP [24]. It is also valuable in the differential diagnosis of somatic tumors and ovarian clear cell carcinoma [25]. In the present case, the immunohistochemically positive SALL4 staining in the tumor cells was instrumental in confirming the diagnosis of pure-type ovarian YST.

4. Conclusion

An extremely rare case of ovarian YST with adnexal torsion in a postmenopausal woman is presented. Markedly elevated serum AFP levels and preoperative imaging suggested torsion and dissemination, prompting semi-urgent surgery for suspected ovarian cancer. Histological and cytological examinations confirmed a yolk sac tumor with omental dissemination. Immunohistochemistry demonstrated SALL4 positivity and loss of PTEN expression. The final diagnosis was torsion of a pure-type YST arising from the left ovary, staged as pT3CN0M0. The patient received BEP and subsequently PC-Bev as adjuvant chemotherapy. Four months after surgery, she remains free of recurrence or relapse.

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us to improve the manuscript. The written consent was approved by the patient before writing this case report.

Ethical Approval

The ethical approval of our hospital was obtained the ethical committee before writing this case report (ethical approval no. 26022711).

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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Abbreviation

YST	Yolk sac tumor
AFP	α-fetoprotein
PTEN	Phosphatase and tensin homolog
GCT	Germ cell tumors
BEP	Bleomycin, etoposide and cisplatin
PC-Bev	Paclitaxel, carboplatin, and bevacizumab
SALL4	SALL-like protein