EJGO European Journal of Gynaecological Oncology

An unusual ovarian neoplasm diagnosed in a patient with rupture of unicornuate uterus during pregnancy: a case report

T.Y. Liu[1], Y.X. Zhu[2], P.Q. Ke[1], M. He[1], Y.C. Liang[1], S.Z. Yao[1]

[1] Department of Obstetrics and Gynecology, The First Affiliated Hospital of Sun Yat-sen University, Guangzhou
[2] Department of Ultrasonic Medicine, The First Affiliated Hospital of Sun Yat-sen University, Guangzhou (China)

Summary

Unicornuate uterus is a rare disease characterized with reduced fertility, and ovarian tumor diagnosed during pregnancy is uncommon as well. These two diseases have been reported separately. However, patient suffering from both diseases has never been reported before. The authors herein report a case of a 32-year-old Chinese woman presenting with a unicornuate uterus with no horn, who suffered from acute abdominal pain and intra-abdominal hemorrhage at 26 weeks gestation. Incidentally, a borderline ovarian tumor (BOT) and rupture of uterus were found during an urgent exploratory laparotomy. During the follow-up, ovarian tumor recurred in the first year after the operation. The authors suggest that BOT with micropapillary patterns should be paid much more attention to, other than only assessing the histological type. Furthermore, they also suggest that a slightly increased in serum CA-125 value should not be ignored.

Key words: Urogenital abnormalities; Uterine rupture; Pregnancy; Ovarian neoplasms; Recurrence.

Introduction

Unicornuate uterus is one kind of Müllerian anomalies, which arises from the normal differentiation of only one Müllerian duct. Jayaprakasan *et al.* [1] reported that the incidence of uterine anomalies was 13.3%, while the unicornuate uterus accounted for 3.3% of the uterine anomalies. In a ten-year retrospective study, Akar *et al.* concluded that the reproductive performance of women with unicornuate uterus was poor, with a live-birth rate of only 29.2%, prematurity rate of 44%, miscarriage rate of 29%, and ectopic pregnancy rate of 4% [2].

The incidence of ovarian masses combined with pregnancy is 2.4–5.7% [3]. Borderline ovarian tumors (BOTs) are classified within malignant epithelial ovarian tumors, constituting 10–20% of these [4]. Ovarian tumor during pregnancy is rare.

To the best of the authors' knowledge, pregnancy in a unicornuate uterus with ovarian neoplasms has never been reported. Here they first report a case of pregnant woman who suffered from the rupture of unicornuate uterus (B type, Buttram and Gibbons's classification of unicornuate uterus [5]) and ovarian neoplasm simultaneously.

Case Report

A 32-year-old primigravida was admitted at 26 weeks gestation because of a sudden onset of pain that increased over time. The pain began around her navel and then shifted to the right lower abdomen. She did not have a fever, nausea, watery vaginal discharge or vaginal bleeding. Vital signs of the patient were as follows: body temperature 37.8°C, heart rate 80 beat per minute, and blood pressure 110/70 mm Hg. Physical examination revealed abdomen was 26 weeks in size. Meanwhile, she had tenderness, guarding or rigidity, and rebound tenderness of right lower abdomen. Although the left abdomen was soft, there was also a positive tenderness and suspicious rebound tenderness. Laboratory tests were normal, except moderate decreased hemoglobin (78.0 g/L), neutrophil granulocyte increased to 82.1%, platelet elevated to 358×10^9/L. Ultrasonography displayed a sign of ascites (the maximum depth of fluid sonolucent area was 7.7 cm), indicating a possibility of hemoperitoneum (Figure 1A). Live singleton gestation was revealed and the development of the fetus was about 26 weeks gestation. No evidence of obvious placental abruption or placenta accrete (Figure 1B) was shown. In view of these features, she was suspected to have acute peritonitis. Acute appendicitis during pregnancy and intra-abdominal hemorrhage were also taken into consideration. An urgent exploratory laparotomy was performed due to the increasing abdominal pain of the pregnant woman. More than 3,000 ml of hemoperitoneum was removed and active bleeding from the uterine rupture site was noted. The uterus was about six month's gestation in size and out-of-shape. The right fundus projected obviously with very thin muscular layer, which displayed bluish appearance and had three rupture sites (0.5 cm in diameter respectively) with active bleeding. During the surgery only the left adnexa was found and the patient was diagnosed with rupture of unicornuate uterus with intra-abdominal hemorrhage. A male infant was delivered, however, without vital signs. After intravenous oxytocin infusion there was no sign of placental separation. The placenta adhered tightly to myometrium of the right fundus. Subsequently, subtotal hysterectomy was performed due to placenta accreta. Left hydrosalpinx was found and the left ovary was wrapped in the left fallopian tube. A small papillary neoplasm was found on the surface of the left ovary, with a size of 2×2 cm. According to the requirement of her family, the authors opted for an ovary-sparing surgery. Post-

Revised manuscript accepted for publication August 4, 2015

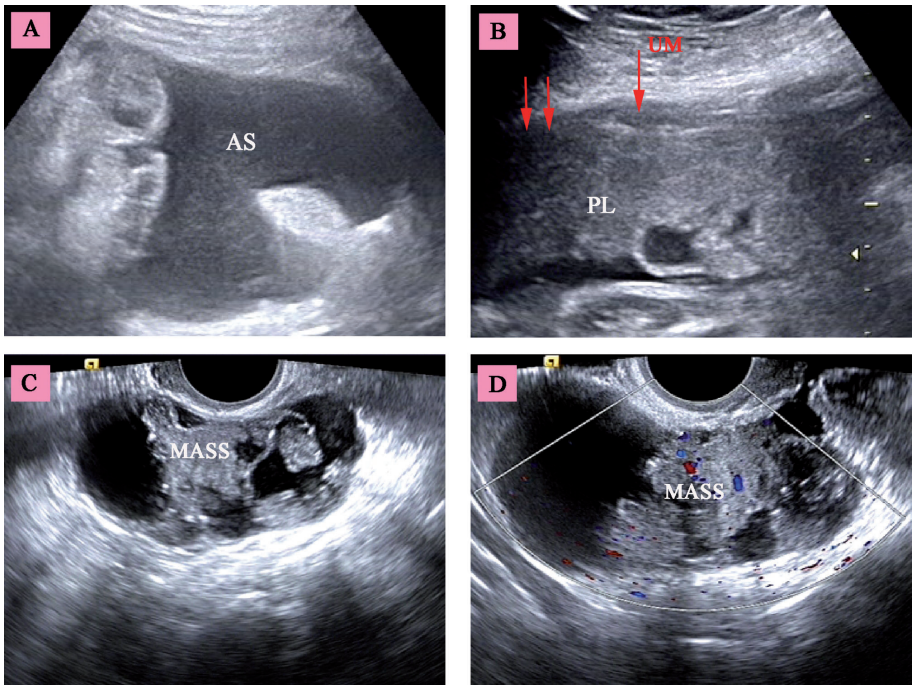

Figure 1. — Ultrasound findings before the initial operation. A) AS (ascites). B) PL (placenta). The UM (uterine myometrium) that the middle arrow indicates a clear low echo. The left two arrows indicate the right cornua uteri, whose myometrium is unclear. C) and D) The ultrasound findings before the second operation. There is a solid-cystic mass of the left ovary. D) Image of color Doppler, in which blood flow signals in the mass can be found.

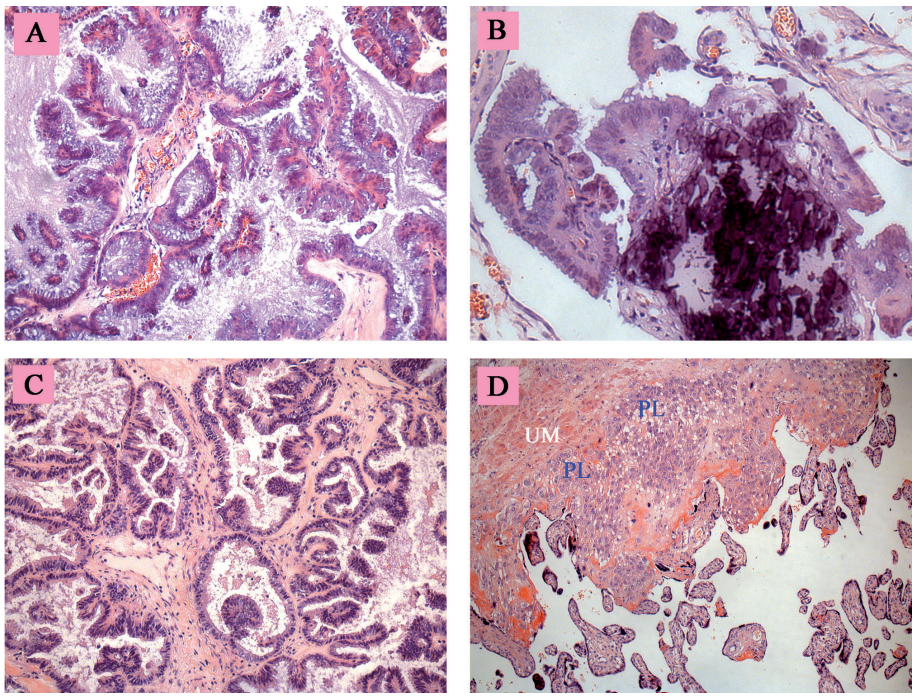

Figure 2. — A) Serous borderline ovarian tumor (S-BOT) found in the primary operation, in which many papillae with irregular contours can be seen (HE×20). B) Invasion of the cystadenoma cells in fiber connective tissue near the oviduct (HE×40). C) S-BOT found in the second operation, in which many papillae with hierarchical branching can be seen (HE×20). D) Placenta accreta (HE×20). UM (uterine myometrium), and PL (placenta).

operative pathological examination revealed placenta accreta and borderline micropapillary serous cystadenoma with malignant transformation locally of the left ovarian (Figures 2A and 2D). Microscopically, regarding the ovarian lesion, stromal invasion was found locally, which was no more than 0.3 cm. Furthermore, invasion of the cystadenoma cells was found in fiber connective tissue near the oviduct, which was considered resulting from the dissemination of the ovarian tumor (Figure 2B). Total blood loss was 4,500 ml. The lady was transfused with 1,600 ml of concentrated red blood cells and 1,400 ml plasma. Postoperative blood analysis showed an elevated level of CA-125(181.7 U/ml, normal range: 0-35 U/ml), while the levels of CEA, CA19-9, and SCC were all within the normal range.

The patient received four cycles of combination chemotherapy with paclitaxel and carboplatin. The level of serum CA-125 decreased from 181.7 to 9.3 U/ml. Later multiple re-examinations demonstrated normal CA-125 value. However, nearly one year after the initial surgery (June 11, 2012), transvaginal color

Doppler ultrasound showed a solid-cystic mass (5.9×4.7 cm) in the left ovary, which suggested tumor recurrence. Until the third year after the surgery, multiple ultrasound re-examinations showed the imaging result was similar to the result on June 11, 2012. Therefore the patient paid no attention to her disease and did not receive any treatment after the initial surgery. But half year later (January 8, 2015), the tumor enlarged to 8.5×5.5 cm in size (Figures 1C and 1D). Meanwhile, the serum CA-125 value increased from 7.1 to 33.7 U/ml. Thus the second operation was conducted. During the operation, no ascites or obvious implant lesions were found. Frozen section reported borderline papillary serous cystadenoma of the left ovary. Subsequently, the woman received a comprehensive staging surgery. Macroscopically, the solid-cystic mass was cauliflower-like with papillae of the left ovary. Microscopically, borderline papillary serous cystadenoma (Figure 2C) with stromal invasion locally (no more than 0.3 cm) was found, however without lymph node metastasis. Considering the guidelines of BOTs in National Comprehensive Cancer Network (NCCN) and the conditions of the patient, postoperative chemotherapy was not prescribed. Three months after the second surgery, imaging test demonstrated unremarkable ultrasound, and blood test revealed a normal level of serum CA-125 as well.

Discussion

This is an interesting case because the small ovarian neoplasm was discovered during the operation for rescuing the pregnant woman who suffered from the rupture of her unicornuate uterus at 26 weeks gestation.

A French retrospective multicenter study of 40 patients with BOTs diagnosed during pregnancy reported the tumor size ranged from 1.5 cm to 30 cm [6]. The size of ovarian neoplasm in the present case was 2×2 cm, which was within the range of tumor size reported by the French study described above. However, the woman did not have prenatal examinations. Whether the neoplasm occurred before or after the pregnancy is unknown. It was also too small to be discovered easily by the emergency ultrasound examination, especially during pregnancy. Fortunately, the operator was so careful that the small ovarian neoplasm was discovered.

In the present case, an ovary-sparing surgery was conducted. Would the type of surgery affect the recurrence rate? Some studies revealed that the rate of recurrence tended to be higher following cystectomy than unilateral salpingo-oophorectomy (USO). Morice *et al.* [7] discovered cystectomy had higher recurrence rate than USO (36.3% *vs.* 15.1%). Vasconcelos *et al.* [8] lately noted that cystectomy in unilateral serous BOT was significantly associated with a higher recurrence rate, but with no impact on survival. However, most studies demonstrated the recurrence rate in the fertility-sparing surgery does not differ significantly by the type of surgery (USO or cystectomy), and cystectomy can be considered for patients with bilateral tumors or previous USO [9-12].

In this case, histological type had a micro-papillary pattern. Shih *et al.* reported that two pathological parameters, including invasive implants and micropapillary histology, were clinical factors associated with increased risk of recurrence in women with BOT. They found the micropapillary pattern was associated with low disease-free survival of 75.9%, compared with 94.3% for patients without a micropapillary pattern [12]. Otherwise, Bell *et al.* revealed that BOT with micropapillary patterns seems to be more related to presence of invasive implants rather than to this particular histological feature [13]. May *et al.* discovered that the gene-expression profile of serous lesions with micropapillary patterns was similar to that of invasive low-grade serous carcinoma, but distinct from that of serous BOTs [14]. All those suggest BOTs with micropapillary patterns may have poorer prognosis than do lesions without this histological feature. Furthermore, stromal invasion appears more frequently in serous BOT. In this case, borderline ovarian serous cystadenoma with stromal invasion (less than 0.3 cm) can be found locally in the ovarian lesion. Morice *et al.* [15] reviewed previous literatures and indicated that microinvasion is a prognostic factor for serous BOTs. With regards to the present case, combining with these findings and the pathological results of the two operations, the authors considered that the histopathological type was a risk factor leading to the recurrence, other than the type of surgery.

Faluyi *et al.* [16] reported that no evidences supported the use of any specific type of adjuvant therapy for BOTs. NCCN 2015 noted the significance of postoperative chemotherapy had not been demonstrated for patients who had no invasive implants. There is no consensus regarding standard therapy for the group of patients with invasive implants (BOTi). A French scholars conducted a retrospective study in 2013 and they showed a possible role for adjuvant chemotherapy in BOTs with invasive implants [17]. On the contrary, a meta-analysis performed by German scholars Vasconcelos *et al.* revealed that the recurrence rate was 44.0% (95% CI: 0.354-0.529) for patients with BOTi (n=162) undergoing adjuvant treatment and 21.3% (95% CI: 0.087-0.435) for patients undergoing upfront surgical treatment. The reduced recurrence rate was not statistically significant ($p = 0.114$) [18]. After the initial surgery, pathological examination revealed borderline micropapillary serous cystadenoma with local malignant transformation. Otherwise, invasion of the cystadenoma cells could be found in fiber connective tissue near the oviduct. Consequently, four cycles of combination chemotherapy were performed. With regards to the recurrence of the present case, the authors chose a comprehensive staging surgery without postoperative chemotherapy. On the one hand, although the patient was only 38-years-old, she did not desire to maintain her fertility due to the removal of her uterus in the initial operation. On the other hand, no obvious implant lesions were found in the second surgery and the frozen section reported borderline papillary serous cystadenoma of the left ovary.

There are no available markers having a diagnostic and

prognostic significance of ovarian tumor in pregnancy. Serum CA-125 in pregnancy has limited value because it fluctuates widely in normal pregnancy. Previous studies suggested that CA-125 is found at high levels during the first trimester and then returns to normal [19]; however CA-125 is still the most common biomarker that is used for diagnosis and prognosis of epithelial ovarian tumor. Shih *et al.* found that preoperative CA-125 was significantly associated with prognosis [12]. In the present case the pregnant woman had an increased CA-125 value at the second trimester. Regrettably, this patient did not have a systematic examination before pregnancy, and thus the authors were unable to make a comparison before and after she was pregnant. What was worse, according to the patient's condition, the authors were not aware of BOT preoperatively. As a result, they did not test the serum CA-125 before the initial operation. Anastasi *et al.* [20] indicated that we should not overlook even a slight increase of CA-125 in the presence of a BOT as it could be an indication of a progressive disease. With regards to the present case, after the first operation, the patient received chemotherapy. Her serum CA-125 value returned to normal after the second cycle. Recurrence accompanied with the serum CA-125 elevated slightly from 7.1 to 33.7 U/ml. These data may again suggest that we should not ignore a slight elevated serum CA-125 value.

Unicornuate uterus is a rare disease, and ovarian tumor diagnosed during pregnancy is uncommon as well. Here the authors first report a patient who suffered from both diseases. It is emphasized once again the importance of systematic prenatal examinations. Meanwhile, carefulness and earnest for an operator are absolutely important as well. In the present case, the operator was so careful that the small ovarian neoplasm was discovered at an early stage. The present authors also consider that the histopathological type is more likely to be a risk factor leading to recurrence than the surgical approach. The authors suggest that BOT with micropapillary patterns should be paid much more attention to, other than only assessing the histological type. Furthermore, they also suggest that a slightly increased in serum CA-125 value should not be ignored.

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Address reprint requests to:
S.Z. YAO, M.D.
The First Affiliated Hospital of
Sun Yat-sen University
No.58 Zhongshan 2nd Road
Guangzhou 510080, Guangdong (China)
e-mail: yszlfy@163.com