

Case report

Enlarging ovarian cysts mimicking malignant or borderline tumors during pregnancy

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ARTICLE INFO

Keywords:

Ovarian cyst
Pregnancy
Pregnancy complication
Endometrioma
Decidualization
Case report

ABSTRACT

Background: Ovarian cysts are uncommon gestational complications. Because of high-level progesterone, ovarian endometriomas may undergo decidualization during pregnancy, manifesting as enlarging cysts with papillae and rich blood flow. Such cases can mimic malignant or borderline tumors, causing dilemmas in clinical management. Here, we present two cases of enlarging ovarian cysts during pregnancy with evidence suggesting decidualized endometrioma. The diagnosis and treatment are further discussed, which add to our limited knowledge and might help future clinical practice.

Case summary: In the first case, a right ovarian cyst was detected by ultrasound in a 32-year-old pregnant woman. The cyst measured 4.2 cm in diameter at 7⁺⁶ weeks of gestation, and gradually increased to 9.6 cm × 7.6 cm × 5.6 cm at 37⁺⁵ weeks, with multiple solid papillae lining the inner wall. During cesarean section, an ovarian mass of approximately 9 cm in diameter was surgically removed, which was later identified by pathological review as an endometrioma with decidualization. The second case also presented as an enlarging ovarian mass during the first and second trimester. The size of the cyst peaked at 24⁺⁵ weeks of gestation, measuring 6.9 cm × 5.6 cm × 4.1 cm. But in the third trimester, the tumor slightly regressed. Careful follow-up was adopted after successful vaginal delivery, and the cyst was found to have undergone quick regression shortly after pregnancy. Both patients recovered well after delivery with no further complications.

Conclusion: Endometriomas with decidualization during gestation may resemble borderline or malignant tumors. Close monitoring and proper management are essential for guiding clinical management.

1. Introduction

Based on previous studies, ovarian cysts occur in approximately 0.05–5% of pregnancies.^{1–5} The broad application of ultrasound in obstetrics has significantly enhanced the diagnostic rate of ovarian cysts during pregnancy, and also provides important clues for clinical decision-making. In most cases, ovarian cysts present as benign or physiological cysts that generally regress spontaneously and seldomly cause severe symptoms. For persistent ovarian cysts during pregnancy, only about 1%–6% could finally be demonstrated as malignant⁶, leading to an overall incidence of ovarian cancer being lower than 50 per million pregnancies.^{5,7} Among ovarian cancers during pregnancy, germ cell

tumors were identified as the most common pathological type.⁸ Doctors will usually raise doubts about the nature of the cysts when they present as giant or enlarging masses, thus causing a dilemma in clinical management due to difficulties in balancing the oncological safety and potential risks to the mother and fetus brought by surgical treatment.

Here, we present two cases with enlarging ovarian cysts during pregnancy, one of which was finally demonstrated by pathological review to be endometriotic cyst with decidualization, and the other gradually regressed during late pregnancy and the postpartum period. Some related studies are also reviewed.

This study was approved by the Institutional Review Board of Peking University People's Hospital (IRB 00001052–19142). Patients' written

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<https://doi.org/10.1016/j.gocm.2021.11.001>

Received 4 April 2021; Received in revised form 1 July 2021; Accepted 1 November 2021

Available online 19 November 2021

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consents were obtained before the study.

2. Case presentation

2.1. Case 1

2.1.1. Chief complaints

A 32-year-old woman was referred as an outpatient at 38⁺³ weeks of gestation due to a gradually increasing right ovarian cyst during pregnancy and paroxysmal lower abdominal pain starting 7 hours prior.

2.1.2. History of present illness, imaging examinations, and laboratory examinations

The ovarian cyst was first found as a 4.2 cm hypoechoic mass under transvaginal ultrasound at 7⁺⁶ weeks of gestation. The mass gradually enlarged during gestation. In the third trimester (37⁺⁵ weeks of gestation), the size of the cyst increased to 9.6 cm × 7.6 cm × 5.6 cm under ultrasound, with multiple solid papillae on the inner wall (the largest one being 2.6 cm in diameter) and septa across the cystic cavity (0.2 cm in thickness). Color Doppler flow imaging (CDFI) revealed a resistance index (RI) of 0.50 and a pulsatility index (PI) of 0.69 in the papillae, suggestive of a borderline tumor (Fig. 1). During pregnancy, the serum α -fetal protein (AFP) was elevated (191.10 ng/ml at 30 weeks and 188.90 ng/ml at 38⁺⁴ weeks, normal range <7.00 ng/ml), but no significant alterations of serum carbohydrate antigen (CA) 125, CA 19-9, or CA 72-4 were found. No apparent abdominal symptoms were reported from the patient during routine check-ups in middle and late pregnancy. The patient was admitted as an inpatient for threatened labor at 38⁺³ weeks.

2.1.3. History of past illness

The patient had normal menstrual cycles. She received an induced abortion in 2011 and this was her second time of gestation.

2.1.4. Treatment and final diagnosis

We conducted a cesarean section upon the patient's request. A 3880 g male infant was delivered successfully during the surgery. In the surgery, a big cyst about 9 cm in diameter was observed on the right ovary, adhering to the right uterosacral ligament and the posterior lobe of the right broad ligament. Brown viscous liquid was seen when tearing apart the cystic wall. Intraoperative freezing section showed no evidence of malignancy in the cystic wall. The cyst was completely resected and sent for routine pathological evaluation. In addition, peritoneal washing was also collected and sent for cytological examination. In the pathological review, an endometriotic cyst with decidualization was observed, and no positive findings were reported in peritoneal cytology. The patient was discharged from hospital 4 days after surgery.

2.2. Case 2

2.2.1. Chief complaints

The second case was a 33-year-old who was admitted as an inpatient at 39⁺⁶ weeks of gestation for a left ovarian cyst and suspected oligohydramnios (with an amniotic fluid index of 4.8 cm).

2.2.2. History of present illness, imaging examinations, and laboratory examinations

During pregnancy, a former existing ovarian cyst gradually increased in the first and second trimester of gestation. At 12 weeks of gestation, the cyst was 4.1 cm × 3.9 cm. At 24⁺⁵ weeks of gestation, the cyst increased to 6.9 cm × 5.6 cm × 4.1 cm, with multiple papillae lining the uneven inner wall, the largest being 2.7 cm in diameter (Fig. 2A&B). At 29⁺⁴ weeks of gestation, a magnetic resonance imaging (MRI) scan showed a 6.0*2.5*4.5 cm multi-cystic tumor in the left ovary clearly separated from surrounding tissues, with several nodular protrusions along the margin (Fig. 2C&D). The cystic components showed short T1 and long T2 signals, and high signals in diffusion-weighted imaging (DWI), suggestive of benign tumors including endometriosis. At 34⁺³ weeks, the B ultrasound showed a left ovarian mass of 6.7 cm × 5.5 cm × 2.3 cm in size, with multiple papillae and septa. CDFI showed blood flow in the papillae, with RI 0.46–0.67, and PI 0.65–1.04. Change in cyst size during gestation is shown in Fig. 3A. During pregnancy, the serum tumor markers AFP (ranging from 210.50 to 295.40 ng/ml), CA 125 (29.35–123.30 U/ml, normal range: 0–35.00 U/ml), and CA 19-9 (25.82–56.30 U/ml, normal range: 0–39.00 U/ml) all increased to different extents (Fig. 3B). There were no self-reported symptoms from the patient throughout the gestation.

2.2.3. History of past illness

The patient had normal menstrual cycles before pregnancy, and this was the first time of gestation. She had experienced biochemical pregnancy one year ago and been found to have a 5.5 cm × 4.3 cm left ovarian cyst suspected to be an endometrioma in B ultrasound at the same time. She did not receive further examination or treatment.

2.2.4. Treatment and final diagnosis

Based on the evidence above, a diagnosis of endometrioma was suggested. Since borderline or malignant tumors could not be completely excluded, serious discussions were conducted with the patient and expectancy was adopted. The patient had successful vaginal delivery at 40⁺¹ weeks of gestation, giving birth to a 3640 g mature male infant, and was discharged from the hospital 3 days after delivery.

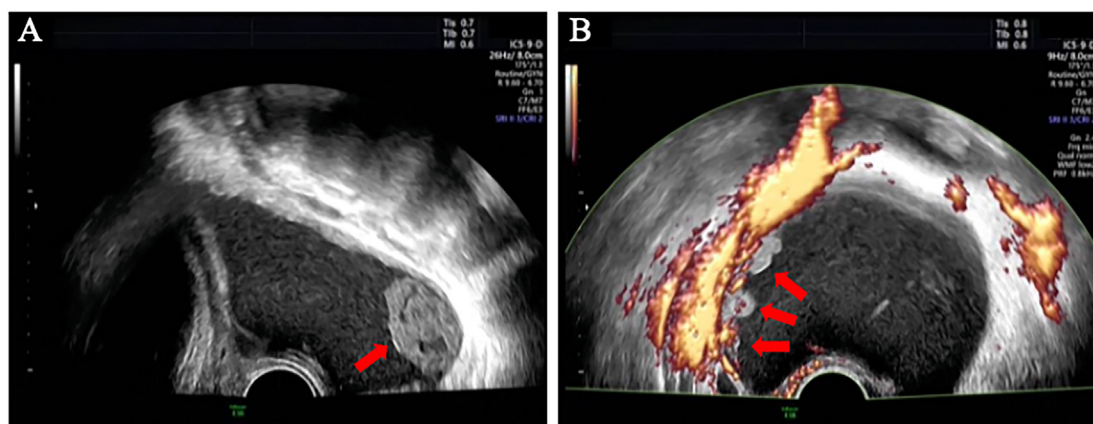


Fig. 1. Left ovarian cyst of case 1 at 37⁺⁵ weeks of gestation under ultrasound.

A. Ultrasound presentation of the cyst. B. CDFI features of the cyst. Red arrows indicate the papillae.

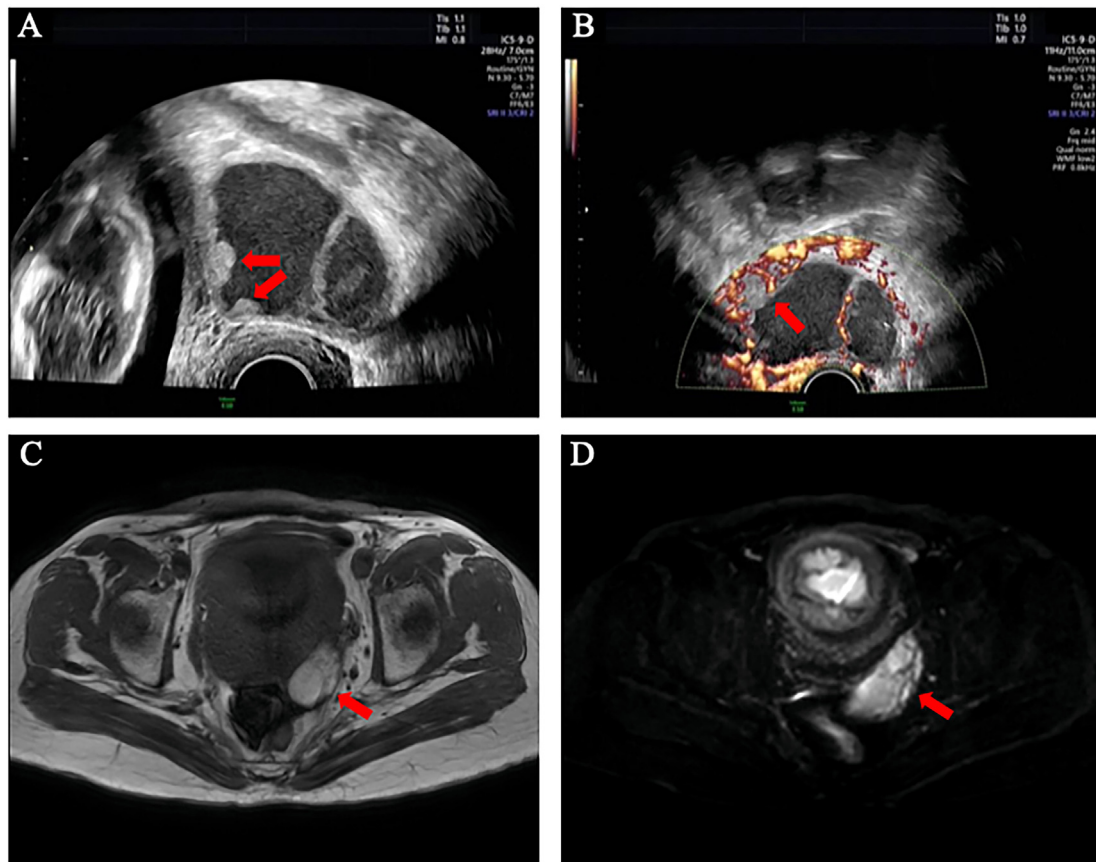


Fig. 2. Right ovarian cyst of case 2 at 24⁺⁵ weeks of gestation. A, B. Ultrasound presentation of the cyst. Red arrows indicate the papillae. C. T2-weighted imaging of the cyst. The red arrow indicates the cyst. D. Diffusion-weighted imaging of the cyst. The red arrow indicates the cyst.

2.2.5. Outcome and follow-up

Ultrasound was used to follow up on this patient in the outpatient clinic. At one month after delivery, the cyst spontaneously regressed to 2 cm. Three months after delivery, the size of the mass further decreased to 1.4 cm, with all tumor markers returned to normal ranges.

3. Discussion

In this case report, two cases with ovarian cysts gradually increasing in size with gestational age were reported, both accompanied by the increase of one or more serum tumor markers. Surgery was conducted in case 1 and conservative management was used in case 2. Both cysts were finally identified as benign by clinical or pathological evidence. Currently, international consensus or guidelines regarding the

management of ovarian tumors during pregnancy are still limited. Recently, a guideline on gynecologic cancers in pregnancy by European gynecologic oncologists was published⁷, followed by a consensus on the management of ovarian masses during pregnancy by Chinese experts.⁹ But further discussions on diagnosis and treatment strategies are still needed for better individualized care of these ovarian cysts.

According to previous studies, ovarian masses were most commonly detected in the first trimester of pregnancy¹⁰, possibly due to the advent of ultrasound during routine check-ups and the relatively higher frequency of torsion during this period.⁵ But sometimes they can be detected during caesarean sections or in the postpartum period.¹¹ Generally, ovarian masses during pregnancy will seldom cause severe clinical symptoms, unless complications like torsion or rupture occur.^{5,12} Occasionally, large cysts may cause obstructive symptoms due to

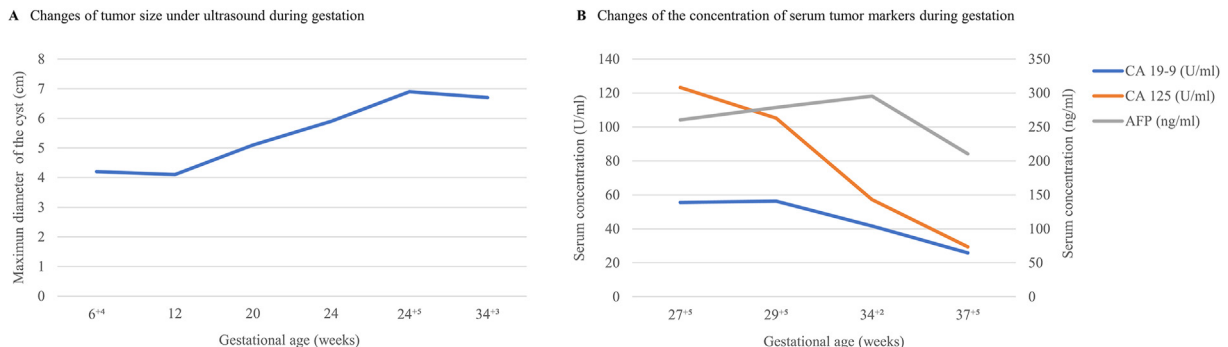


Fig. 3. Changes in cyst size and serum tumor markers during gestation in case 2.

compression of the digestive tract or ureter, and may even be associated with labor obstruction.^{5,12} Recently, Kiemtoré et al.⁴ reported a rare case manifesting as persistent abdominal distension after delivery, that was later demonstrated by surgery to be a serous ovarian cystadenoma of 42 cm in the long axis. In the two cases reported here, both patients were asymptomatic and the cysts were detected by ultrasound in the first trimester, which was similar to most cases reported before.^{11, 13}

The differential diagnosis of the cases included endometrioma, borderline tumor, and ovarian cancer. In a recent case series including 53 ovarian cysts suspected to be an endometrioma under ultrasound, 15 were monitored until the postpartum period, of which nine (60%) disappeared.¹³ In another study of 26 published cases, all eight cysts with conservative management resolved following delivery.¹⁴ In our report, one cyst also underwent spontaneous resolution during the late-pregnancy and postpartum period, but the other presented as an enlarging cyst. In the case series by Bailleux et al.,¹³ of the ten cysts surgically removed, only four were proved to be endometriomas by pathological examination, with the others being serous cystadenoma, mucinous cystadenoma, or dermoid cyst¹³, indicating the difficulty of diagnosis during pregnancy. Decidualization of endometriomas, a relatively rare condition induced by high progesterone levels during pregnancy, further raised challenges to clinicians due to similarities to malignant tumors under ultrasound.^{14–16} In studies analyzing ultrasonographic features of decidualized endometriomas during pregnancy, most cysts showed papillary projections, and rounded projections with vascularization was shown to be a vital feature,^{16–18} consistent with our two cases. However, in an imaging study¹⁶, only 22% of the cases showed more than three papillary projections in the cyst, while in our study, a multiple-papillary feature was seen in both cases.

Serum tumor markers provide very important clues for tumor properties. Nevertheless, some tumor markers like CA 125 and AFP could be elevated during pregnancy, especially in the first trimester^{19–21}, making it difficult to accurately diagnose a malignancy. An earlier study conducted by Aslam et al.²² suggested CA 125 concentration of 112 U/ml to be a cut-off value for determining cyst properties in pregnant women. In our first case, only serum AFP was elevated, and in the second case, AFP, CA 125, and CA 19-9 all increased to different levels. Though CA 125 increased to 123.3 U/ml at 27⁺⁵ weeks in the second case, it then gradually decreased. Moreover, evidence from ultrasound and clinical manifestations further supported the diagnosis of a benign tumor. Therefore, the clinical significance of tumor markers should be determined based on the dynamic changes during pregnancy and in combination with other evidence.

In the recently published Chinese consensus for the management of ovarian cysts during pregnancy (9), for tumors 5–10 cm in diameter without evidence supporting malignancy, expectancy was recommended, and surgery indications included acute complications (including rupture and torsion), complication caused by obstruction (e.g. hydronephrosis), risk of birth canal obstruction, and strong evidence of malignancy. The recommended surgery time included 14–24 weeks of gestation, surgery during cesarean section, and 6 weeks postpartum. In the first case, imaging evidence including a relatively high speed of growth, multiple-papillary feature, and blood flow detected inside the cyst made it hard to completely exclude malignancy, though a higher probability of decidualized endometrioma was suggested, as mentioned above. A cystectomy during cesarean section was performed, though the tumor size was still below the 10 cm cutoff recommended by the consensus. For the second case, though multiple papillae and blood flow signals were observed, the relatively small diameter (<10 cm) and stabilization of tumor size in the third trimester helped us to determine that the cyst was not cancer, and a rapid regression observed during the follow-up after delivery further supported our assumption of the tumor as benign.

One strength of our study is that both cases were carefully monitored during gestation, making it feasible to notice any changes of the tumor and deliver treatment accordingly. Detailed ultrasound features of the two cases were studied, which may be helpful for future practice. But

unfortunately, in the second case, pathological evidence to confirm our diagnosis was not obtained.

4. Conclusion

This report provided two cases from our center with enlarging adnexal masses during pregnancy, which mimicked borderline or malignant ovarian tumors and caused dilemmas in clinical management. Ultrasonographic features and pathological examination supported both cysts as endometriomas with decidualization, a relatively rare condition. Currently, research findings about the clues for its clinical diagnosis are still limited. Careful ultrasound monitoring during pregnancy is currently essential for differentiating these endometriomas from malignancy, and follow-up after delivery in cases treated with expectancy may better reveal tumor properties due to the weakening of the effect of progesterone. Still, more studies are needed to fully understand the features of decidualized endometrioma, such as imaging features, natural history, and specific serum biomarkers, for better clinical decision-making.

Author contributions

DY: Reviewed the literature, wrote the manuscript and prepared the figures. LG: Led the surgery, followed up the patients and revised the manuscript. WY and WJ¹: Reviewed the literature and supervised the writing. WZ and WJ²: Acquired the funding and revised the manuscript. All authors approved the final version of the manuscript as current form.

Declaration of competing interest

The authors declare that they have no conflict of interest.

Acknowledgement

This work was supported by the National Key Technology R&D Program of China (2019YFC1005200 and 2019YFC1005201).

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