



Case Report

Hyperreactio luteinalis mimicking malignancy during pregnancy with elevated CA-125

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ABSTRACT

Objective: To report a case with benign bilateral ovarian tumor during pregnancy mimicking malignancy. **Case report:** A 32-year-old women at 20 weeks gestation with large bilateral adnexal masses found on prenatal ultrasound. The cysts had been growing gradually over the course of the pregnancy. MRI show huge multiple cysts in both ovaries. CA-125 was elevated at 260 U/mL. Due to initial impression was malignancy, an excisional surgery was done. Pathology revealed multiple luteinized granulosa cells with benign nature.

Conclusion: Hyperreactio luteinalis (HL) is often asymptomatic and discovered incidentally on ultrasound or at the time of cesarean section. As the lesions are self-resolving, management is conservative and surgical intervention is required only in cases with severe complications. HL can be mistaken for malignancy, especially in cases in which the tumor marker CA-125 is elevated, leading to inadvertent surgery.

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Introduction

Hyperreactio luteinalis (HL) is a rare ovarian cyst occurring pregnancy that is characterized by bilateral ovarian enlargement with multiple benign cysts. While the cause of HL is unknown, the formation of large theca lutein cysts in HL is thought to be associated with high serum level of human chorionic gonadotropin (hCG) or increased ovarian sensitivity to hCG causing elevated ovarian androgen production [1–3]. Of the approximately 100 cases published, many have been reported in patients who were multiparous, had trophoblastic disease, or had received infertility treatment [1,2]. However, HL has also been reported in primiparous women and in spontaneous singleton pregnancies with normal hCG levels [3,4]. As patients may be asymptomatic, HL is most often detected incidentally on ultrasound during the third trimester or at the time of cesarean section [1]. In more recent literature, cases have been reported relatively earlier in pregnancy, likely due to advances in imaging [4].

HL, ovarian hyperstimulation (OHSS), and ovarian cancer should be among the conditions considered in the differential diagnosis of pelvic masses. While OHSS follows fertility treatment, mainly occurs in the first trimester, and is characterized by fluid shift, HL is typically not associated with these features [5]. OHSS and HL both resolve spontaneously, however, whereas malignancy requires intensive treatment. Therefore, consideration of ovarian cancer is reasonable and necessary in patients presenting with bilateral multicystic ovarian enlargement [6]. Herein we report a rare case of HL detected in a patient at 20 weeks gestation with elevated CA-125 which mimicked malignancy.

Case report

A 32-year-old primigravida presented to our clinic at 20 weeks gestation with large bilateral adnexal masses found on prenatal ultrasound. The singleton intrauterine pregnancy was spontaneously conceived. The patient experienced menarche at age 12, had an irregular menstrual cycle, had no personal or family history of ovarian malignancy, and had no history of surgery. Results of pap smear performed one year prior was normal. No anatomical malformation of the fetus was found on ultrasound. Prenatal tests were negative for thalassemia, syphilis, and human immunodeficiency

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virus. The cysts had been growing gradually over the course of the pregnancy, according to the patient, and she was experiencing persistent moderate abdominal pain. The masses were not palpable on physical examination.

Transabdominal ultrasound revealed a multiseptated ovarian mass measuring 159 × 103 × 111 mm (Fig. 1). No prominent blood flow was noted on ultrasound. Serum CA-125 was elevated at 260 U/mL (normal < 35 U/mL). Subsequently, magnetic resonance imaging (MRI) of the pelvis revealed marked enlargement of and multiple cysts in both ovaries as well as mild ascites (right ovary, largest diameter 157 mm [Fig. 2]; left ovary, largest diameter 120 mm [Fig. 3]). Due to the presence of bilateral large ovarian masses with persistent abdominal pain and increased CA-125 level, ovarian malignancy was suspected. After thorough discussion regarding fetal risks with anesthesia, including intrauterine fetal death, the patient consented to surgical excision of bilateral ovary due to unbearable pain and suspected malignancy.

The patient underwent laparotomy with a vertical incision to allow for better visualization and extraction of tumor. Peritoneal washing cytology was done with minimal manipulation of the uterus. No adhesion was present around the ovarian masses, and each mass was carefully extracted without rupture. On gross examination, masses were cystic and bleeding on touch (Fig. 4). Bilateral partial oophorectomy was performed and intraoperative frozen section examination showed multiple corpus luteal cysts composed of luteinized granulosa cells in the stroma and luteinized theca interna cells in the inner layer. Focal hemorrhage was noted, but no malignancy or papillary lesion was found. Due to the benign nature of the masses, surgery was ended, and the final pathology report concluded that the masses were corpus lutein cysts. Unfortunately, intrauterine fetal death occurred 10 days following surgery. Autopsy revealed no external anomalies, and visceral organ structure, umbilical cord, and placenta were all normal.

Discussion

HL is a rare benign condition occurring during pregnancy which regresses spontaneously during the postpartum period. The mainstay of treatment for this self-limiting condition is conservative management [6]. Surgical intervention, however, may be required if the patient experiences severe complications, such as ovarian torsion or hemorrhage, or if malignancy is suspected and cannot be excluded based on imaging [1,7]. To avoid potentially unnecessary surgery, evaluation of ovarian masses should include careful imaging, hormone profiling, and assessment of tumor



Fig. 2. MRI T2 Coronal view. A 15.7 cm hyperintense cystic multiseptum mass at right ovary.

biomarkers to thoroughly rule out malignancy. In contrast to malignancy, HL typically presents with high hCG levels, normal levels of tumor biomarkers, and multicystic ovarian lesions without internal mass on ultrasonography and MRI [8]. In addition, 30% of women with HL have been reported to exhibit virilization due to hyperandrogenism, though this was not observed in our patient [4]. Unfortunately, hormone profiling was not conducted for this patient.

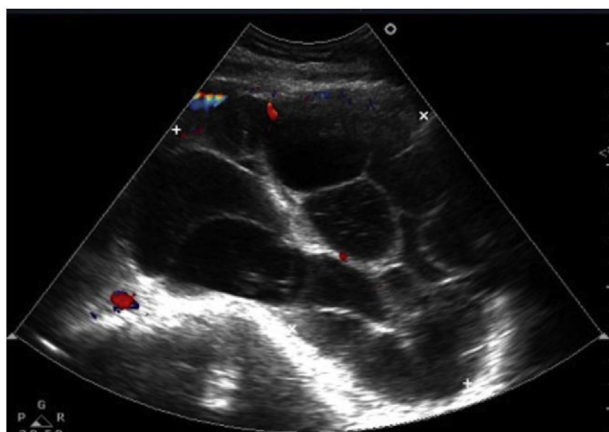


Fig. 1. Transabdominal ultrasound: a multiseptum pelvic cyst (15.9 × 10.3 × 11.1 cm).

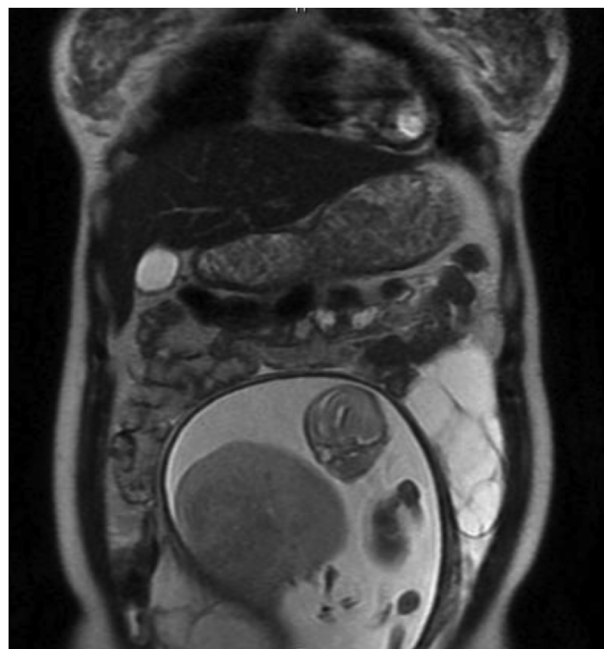


Fig. 3. MRI T2 Coronal view. A 12 cm hyperintense cystic multiseptum mass at left ovary. A fetus in uterus noted.

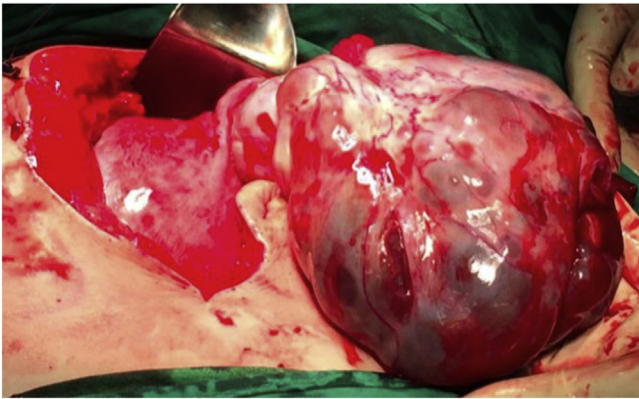


Fig. 4. Intraoperative left ovary. A multicystic and touch bleeding mass (10 cm) was noted.

The suspicion of malignancy was raised in our patient greatly due to her elevated CA-125 level of 260 U/mL. Two cases of HL with elevated CA-125 have previously been reported in the literature [9,10]. In the case reported by Yang et al., CA-125 was 496 U/mL in a patient in whom HL was discovered after delivery of a full-term infant [9]. HL was found at 14 weeks gestation in a primigravida with CA-125 of 442 U/mL in the case reported by Van Holsbeke et al. [10]. Similar to our case, surgery was performed in the latter case due to suspected malignancy, and a diagnosis of HL was made on intraoperative frozen section. While CA-125 is commonly used to help predict the presence of ovarian malignancy, its sensitivity and specificity for discriminating benign from malignant pelvic masses are low [11]. In patients with pelvic masses, CA-125 may be increased as a result of pelvic and peritoneal inflammation [12]. In addition to her elevated CA-125, our patient was experiencing abdominal pain, which ultimately led to our decision to surgically intervene. A recent review found that surgery was performed in 47% of reported HL cases, 38% of which were cases of suspected malignancy [13].

Prevalence of ovarian mass during pregnancy is 2.3–5.4%. Vast of these masses are functional cyst. Other are benign cyst teratoma, paraovarian cysts, serous cystadenoma, mucinous cystadenoma, endometrioma and malignant tumors [14]. In this case, we performed vertical incision with partial oophorectomy to alleviate patient's abdominal pain. However, optimal surgical management for this case is to perform bilateral ovarian biopsy first then perform adequate surgical management as indicated by biopsy result.

Fetus posed risks for mortality during anesthesia and surgery [15]. First, during anesthesia, certain drugs for anesthesia have teratogenic effect. These drugs had most teratogenic effect in first 60 days of embryo development. A large retrospective review for non-obstetric surgery during pregnancy revealed no statistically difference in stillbirth and congenital malformation comparing surgical to non-surgical group. However, An increased rate of low birth weight and neural tube defect in first trimester were observed in surgical group [16]. Secondly, process of anesthesia may cause transient hypotension leading to hypoxia of fetus. Thirdly, surgical

manipulation may cause premature uterine contraction and uterine vessel contraction leading to fetal death [17]. In this case, unfortunately fetal death occurred after surgery. Fetal circulation might be compromised during anesthesia.

In conclusion, this case highlights the pitfalls of mistaking HL for ovarian malignancy and the importance of increased clinician familiarity with diagnosing HL to reduce unnecessary surgical interventions and prevent surgery-related morbidity.

Conflicts of interests

The authors declare that they have no conflicts of interests.

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