

Appropriate management of Huge ovarian cysts during pregnancy. A rare case report and a literature review

Rui Ju¹, Xiangyan Ruan^{1,2}, Alfred O. Mueck^{1,2}

¹ Department of Gynecological Endocrinology, Beijing Obstetrics and Gynecology Hospital, Capital Medical University, Beijing, China

² Department of Women's Health, University Women's Hospital, University of Tuebingen, Tuebingen, Germany

ABSTRACT

In this article, the clinical characteristics of and treatment strategies for hyperreactio luteinalis (HL) are described and discussed. The authors report the case of a woman with huge ovarian cysts that developed during pregnancy. This aim of this report is to increase awareness of HL among obstetricians and gynecologists. The authors recommend individualized treatment strategies and reduction of unnecessary surgical interventions.

KEYWORDS

Hyperreactio luteinalis, pregnancy, management.

Introduction

According to recent reports, the incidence of adnexal masses in pregnancy ranges from 1 in 76 to 1 in 8000 pregnancies [1-3]. The widespread use of early antenatal ultrasound in the first trimester of pregnancy enables early detection of asymptomatic and once clinically undetectable adnexal masses [4]. Treatment of adnexal masses is dependent on the symptoms, with abdominal pain and ovarian torsion constituting the main emergency situations. Large masses are associated with increased risk of torsion, rupture, and dystocia. Surgical treatment is indicated in cases of acute abdomen, severe clinical manifestations (e.g., hydronephrosis), strong suspicion of malignancy, or anticipated risk of dystocia [5]. However, surgery in pregnancy carries some risks such as fetal loss, preterm contractions, and an increased risk of embolic events [5]. Furthermore, most adnexal masses in pregnancy are functional and asymptomatic, and spontaneous resolution will occur in about 31 to 72% of masses [6].

We report the case of a 32-year-old patient in the first trimester of pregnancy with huge ovarian cysts. This report aims to increase awareness of hyperreactio luteinalis (HL) among obstetricians and gynecologists. Conservative management would be better for patients with asymptomatic HL in pregnancy.

Case Report

A 32-year-old primigravida woman presented to our department for prenatal care at 7⁺¹ weeks' gestation. Transabdominal ultrasonography examination revealed huge multicystic ovarian masses with a "spoke wheel" appearance and without solid components. Specifically, she had a cyst measuring 13.0×9.8×7.8 cm on the right ovary and another with a diameter of 2.9 cm on the left ovary.

The patient had previously visited our Department of Gynecological Endocrinology, on March 19, 2018, because of infertility despite having tried for two years to get pregnant. On that

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Contact

Ruan Xiangyan; ruanxiangyan@163.com

Director of the Department of Gynecological Endocrinology, Beijing Obstetrics and Gynecology Hospital, Capital Medical University, Beijing, China

occasion, she complained of irregular menstrual periods. Her last menstrual period dated back to Dec. 3, 2017. Bilaterally, she showed polycystic ovaries but no adnexal masses as monitored by ultrasound. Her height, weight, waist circumference and hip circumference were measured as 158 cm, 65 kg, 78 cm and 89 cm, respectively, and her body mass index (BMI) was 26.04 kg/m². Laboratory data recorded on March 22 are shown in table 1. Total testosterone, and especially free testosterone, levels were increased, but the patient did not present clinical signs of hyperandrogenism such as acne. Polycystic ovary syndrome (PCOS) was diagnosed according to the Rotterdam criteria.

Because the endometrium showed some proliferation (0.73 cm), the patient was initially treated with dydrogesterone (10 mg/day) for 10 days to induce a progestogen withdrawal bleed. Thereafter, she was prescribed a combined oral contraceptive (COC) pill containing drospirenone (3mg) and ethinylestradiol (0.02mg) to adjust her menstrual cycle and improve the hyperandrogenemia. We advised the patient to lose weight and tried to motivate her to perform "standardized lifestyle changes", i.e. our routine program for obese PCOS patients. After six months treatment, she had lost 5 kg and had a BMI of 24 kg/m². When the COC treatment was stopped in mid-September, the patient experienced a withdrawal bleed (Sept. 20). The following month she had another menstrual period (Oct 24), but without ovulation as monitored during this cycle by ultrasound. As during all previous ultrasound monitoring, no adnexal masses were seen at this point. In this situation it is routine in our department to start PCOS patients on ovulation induction using letrozole, 5 mg daily, beginning on menstrual cycle day 5 (which in this

Table 1 The patient's hormone levels at the first examination and during pregnancy.

	AMH (ng/ml)	FSH (IU/L)	LH (IU/L)	E2 (pg/ml)	P (ng/ml)	FT (pg/ml)	TT (pg/ml)	SHBG (nmol/L)	TSH (mIU/L)	β-HCG (IU/L)
Mar. 22, 2018	17.15	4.93	11.78	67.46	0.78	10.9	882.66	52.9	2.06	
Nov. 26, 2018, MC:33d		0.36		886.08	>60				2.75	363.4
Dec. 3, 2018, MC:41d				834.24	59.95					5388.9
Dec. 12, 2018, MC:50d				848.36	55.13					34530.1

AMH: Anti-Müllerian hormone; FSH: follicle-stimulating hormone; LH: luteinizing hormone; E2: estradiol; P: progesterone; FT: free testosterone; TT: total testosterone; SHBG: sex hormone-binding globin; TSH: thyroid-stimulating hormone; β-HCG: β- human chorionic gonadotropin

case was Oct 29), for 5 consecutive days, followed by transvaginal ultrasonography every two days to detect ovulation. On the basis of the follicle growth, highly purified menotrophin, 75 IU, was injected intramuscularly on menstrual cycle day 13 for 2 days. Ovulation was observed on menstrual cycle day 17; the largest follicle (right ovary) reached 2.29 cm. On the same day, triptorelin, 0.1 mg, was injected intramuscularly to trigger ovulation. The large follicle on the right ovary disappeared on day 20. Thereafter (starting on Nov.12), we treated the patient with micronized progesterone capsules, 200 mg/day, as luteal support for 14 days. On menstrual cycle day 33 (Nov.26), the patient's urine HCG level already indicated a positive pregnancy test result.

Two weeks later, at 7⁺¹ weeks' gestation (Dec 12) the patient visited our hospital for a routine prenatal check-up. The fetal sac and fetal heart beat could be seen in the uterine cavity, which is consistent with the gestational age. However, for the first time, a huge multicystic ovarian mass as described above (13.0×9.8×7.8 cm, on the right) was detected by transabdominal ultrasonography. In the Obstetrics Department it was debated whether surgery would be needed, also because the patient had an elevated CA-125 concentration:119.6U/L (normal: <30U/L). However, it is well known that pregnancy can account for a mild increase in CA-125. In this situation some obstetric experts recommend surgical treatment to exclude

ovarian malignancy. Nevertheless, because there were no bothersome clinical symptoms like abdominal pain or abdominal distension, and because the patient's CA-125 concentration dropped down to normal values within a few days, we considered it very likely that the huge ovarian cyst was caused by HL. We did not consider this reaction related to the luteal support (micronized progesterone), because this treatment was only given for 14 days; moreover, the patient received a relatively low dosage (200 mg/day), considering that oral progesterone is recommended at 200-300 mg/day during the first trimester of pregnancy [7].

Although the patient was very anxious about the large cyst, we obtained her informed consent to a conservative approach after discussing with her the literature, in which, mostly, no surgical intervention is recommended, but rather regular prenatal examinations with abdominal ultrasonographic monitoring of cysts every 1-2 weeks. The patient did not experience any discomfort during follow-up. Both ovarian cysts soon started to shrink. The specific transabdominal ultrasonography values recorded are shown in Table 2. The first and the last ultrasonographic images of the right ovarian cyst are shown in Figures 1 and 2, respectively. The patient was thereafter continuously followed up (both for development of the ovarian cyst and for pregnancy outcome), and at the time of writing, fetal development was normal.

Figure 1 Ultrasound image of right ovarian cyst on Dec.12, 2018.**Figure 2** Ultrasound image of right ovarian cyst on Feb.27, 2019.

Table 2 Changes in ovarian volume and ovarian cyst diameters during pregnancy as assessed by transabdominal ultrasonography.

	Weeks' gestation	Volume of right ovary (cm ³)	Diameter of largest right ovarian cyst (cm)	Volume of left ovary (cm ³)	Diameter of largest left ovarian cyst (cm)
Dec.12,2018	7 ⁺¹		13.0		3.4
Dec.20,2018	8 ⁺²	15×9.6×7.6	8.2		
Jan.09,2019	11 ⁺¹	9.1×7.6×6.2	6.8×4.7	12.8×10.8×7.3	9.3×6.2
Jan.30,2019	14 ⁺¹	11.9×13.4×6.6	7.9×6.2	4.6×6.9×2.7	2.7
Feb.13,2019	16 ⁺¹		6.7		2.5
Feb.27,2019	18 ⁺¹	9.3×6.2×5.3	4.8×4.6	normal	none

Discussion

The patient here described has a history of PCOS. Before pregnancy no signs of adnexal masses were observed during multiple ultrasound scans. She became pregnant after ovulation induction during luteal phase support with micronized progesterone (200 mg/day). Bilateral multicystic ovarian masses with a “spoke wheel” appearance on transabdominal sonography were first visualized at 7 weeks’ gestation. The patient had no specific symptoms such as abdominal pain and abdominal distention. Serial transabdominal ultrasound assessment demonstrated that the ovarian cysts shrank continuously during pregnancy. Therefore, we were able to conclude that the huge ovarian cysts were caused by a form of HL.

Hyperreactio luteinalis is a rare benign condition characterized by bilateral functional multicystic ovarian enlargement during pregnancy and after delivery, which can regress spontaneously without specific treatment [7]. We reviewed the English literature from PubMed for the past 10 years and found 45 available cases within 32 relevant reports on HL [8–40]. According to those reports, 67% of HL patients were primiparous and 75% of HLs were detected in the second and third trimester. Some case reports showed that HL can also occur in the first trimester and can be recurrent in subsequent pregnancies [17, 18, 21, 31, 33, 39]. It has been suggested that HL can develop secondary due to elevated β -human chorionic gonadotropin (β -hCG) (e.g. as a result of decreased β -hCG clearance due to decreased renal function) or caused by increased ovarian stromal sensitivity to β -hCG [11]. Therefore, HL was considered to be more common in multiple gestation pregnancies, cases of Rh sensitization, twin-to-twin transfusion syndrome, gestational trophoblastic disease (such as molar pregnancy and choriocarcinoma), PCOS and ovulation induction as during clomiphene therapy [37].

Within our literature review, 97% of pregnancies were cases of spontaneous singleton conception, sometimes associated with complications such as thyroid dysfunction, hyperemesis gravidarum, preeclampsia, HELLP syndrome, premature delivery, fetal growth restriction, placental insufficiency and delayed lactation [23, 27, 30]. Notably, many cases present with hyperandrogenism persisting during pregnancy. According to the literature, about 30% of HL cases were asymptomatic [27, 30]; 37% were diagnosed during surgeries like caesarean or wedge re-

section, or oophorectomy due to ovarian torsion, infarction and hemorrhage, or surgery performed to rule out suspected ovarian malignancy [26]. An appropriate diagnosis of HL is important to prevent unnecessary surgical intervention. The widespread availability of antenatal care and advances in imaging techniques enable early detection of adnexal masses in pregnancy [30]. Transabdominal ultrasonography is the preferred diagnostic tool during pregnancy [8, 27]. Magnetic resonance technology may be helpful for the diagnosis of HL to rule out ovarian malignancy [27]. On ultrasonography the presentation of HL is bilateral and multiple, identified by the presence of thin-walled luteal cysts with a typical “spoke wheel” appearance and a lack of solid components and normal Doppler flow sonography, all of these do not show in ovarian malignancies [40].

The fear of missing a cancer diagnosis often leads the physician to opt for unnecessary surgical intervention to treat HL, which could potentially result in impaired future fertility [26]. However, in many cases it was confirmed that HL can disappear spontaneously and does not need any specific treatment except observation [8, 23, 30]. This ‘conservative approach’ has been recommended since 1993 and can now be considered the “state of art” according to many different reports, i.e. unessential surgical excision should be avoided [26, 30, 32, 35, 40]. Considering its benign nature and potential for spontaneous remission, the first aim in reproductive age women should be preservation of ovarian function, which can mostly be achieved, as in our case. Exceptions to this rule could be the threat or occurrence of acute complications such as ovarian torsion, which could be managed by ultrasound-guided percutaneous cyst aspiration to reduce the ovarian volume; this option should be considered before deciding on emergency laparoscopic surgery [32].

Conclusion

In summary, HL is a self-limiting benign condition characterized by enlarged ovaries with multiple cysts. Regular prenatal check-ups must be routine practice, and are indeed important for every pregnant woman. A conservative approach to HL, i.e. no specific treatment except observation, is highly recommended. Greater knowledge of the features of HL is needed in order to minimize unnecessary iatrogenic harm to patients.

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