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## Case Report

# Differential diagnosis of bilateral ovarian masses during pregnancy, and their hormonal effect

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## ABSTRACT

Rapidly enlarging bilateral ovarian cystic masses can be confused with malignant entities. When this happens during pregnancy, benign transient reactivity can present a similar clinical course. Here we describe a 33-year-old woman with hyperreactio luteinalis or multiple gestational theca lutein cysts whose ovaries drastically changed in size peripartum, with concordant changes in human chorionic gonadotropin, thyroid function, and testosterone levels. Management was conservative and the cystic masses spontaneously remitted postpartum. Present work suggested that evaluating the character of the cysts by magnetic resonance imaging and serial assessments of their size and the patient's hormonal levels may assist in diagnosis. Conservative management could be successfully applied in a carefully chosen subset of patients to avoid unnecessary invasive procedures.

**Keywords:** Androgen, Hyperreactio luteinalis, Pregnancy, Thyroid hormone

## INTRODUCTION

Adnexal masses can be encountered in up to about 6.1 % of early pregnant cases.<sup>1</sup> About 48 % could be classified as simple, while the remaining 52 % could be classified as complex masses.<sup>2</sup> One percent of the simple masses are thought to be malignant, while 9 % of the complex masses are regarded malignant.<sup>2</sup> Resolution rate is generally thought to be high, and even complex large cysts more than 5 cm size would regress in 69 % of the cases.<sup>2,3</sup> It is essential to accurately evaluate the masses as for its possibilities of malignancy, rupture, torsion, and labor obstruction.<sup>2</sup> Especially, enlarging ovarian masses can be confused with malignant diseases.<sup>4</sup> Metastatic tumors are not rare, and a delay in diagnosis may lead to poor maternal prognosis.<sup>5</sup> However, benign conditions, such as luteomas and theca lutein cysts, can also occur.

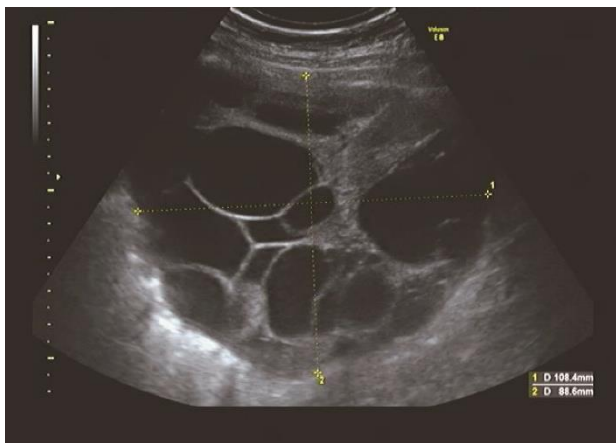
Because of the increase in the number of pregnancies achieved using artificial reproductive techniques and the consequent increase in the incidence of twin pregnancies, these conditions may be more frequently encountered. Knowledge of these rare but benign disease entities, careful differential diagnosis, and management of their endocrinological effects is essential to avoid unnecessary invasive procedures and possible morbidity thereafter.

## CASE REPORT

A 33-year-old gravida 2, para 1 woman was referred to our hospital because of newly detected bilateral ovarian polycystic masses found on the 30th week of her second pregnancy. Her family history was unremarkable. Her past medical history was remarkable only for hypothyroidism, which was well managed with 75 µg

levothyroxine daily. She conceived her first child via artificial insemination by husband, and pregnancy course was uncomplicated. This time, she became pregnant after the first ovulation stimulation. At ninth week of gestation, her ovaries were not enlarged. This pregnancy had been uncomplicated until the 30th week when she was found to have enlarged ovaries. Therefore, she was referred to our hospital for investigating ovarian tumors. Her serum thyroid-stimulating hormone (TSH) level gradually declined from approximately the 12th week. The levothyroxine dose was reduced to 50 µg daily for 1 week before referral as her TSH level dropped to 0.037 µIU/mL (reference range, 0.40-3.80 µIU/mL).

During her first visit to our hospital, abdominal ultrasonography revealed enlarged ovaries measuring 108.4 × 88.6 mm (right) and 89.7 × 99.4 mm (left). They appeared polycystic and septated, with somewhat thick walls (Figure 1).



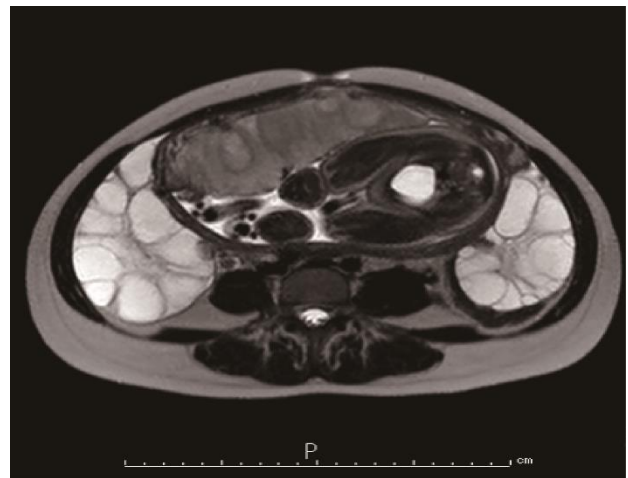
**Figure 1: Ultrasonography showing an enlarged multicystic right ovary measuring 108.4 × 88.6 mm. Although not depicted in this figure, there were some 10-mm-sized nodules within the cysts in other views.**

Fetal growth was appropriate for gestational age. Her serum tumor marker levels for ovarian cancer were not elevated (CA19-9: 5 U/mL, CA125: 45 U/mL). A magnetic resonance imaging (MRI) was performed on the 31st week to assess the character of some nodular part within the cysts, which showed low intensity nodule in high intensity cysts on T2- and diffusion-weighted images (Figure 2), but they appeared low intensity on T1-weighted images (Figure 3); septae were low to iso-intensity in all T1-, T2-, and diffusion-weighted images (Figure 2-4).

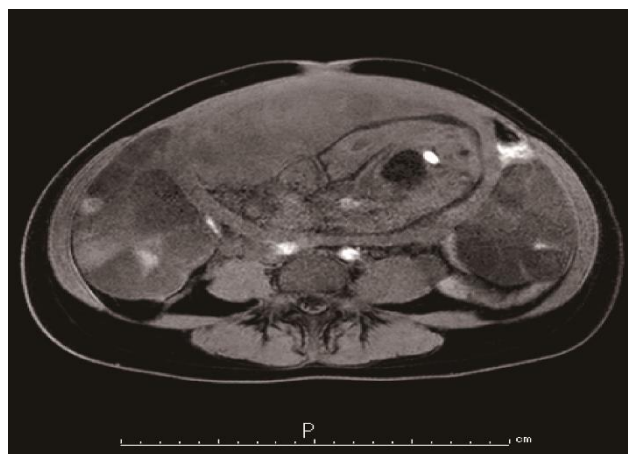
The cysts appeared to be distributed somewhat peripherally in the ovaries. At the 32nd week, her serum human chorionic gonadotropin (hCG) level was highly elevated to 202,736 mIU/mL (reference range, 4,500-90,000 mIU/mL), but the placenta was not thickened and looked normal on abdominal ultrasonography. Although she did not claim any virilizing signs and symptoms, her serum testosterone levels were also elevated to 3.07

ng/mL (reference range, 0.31–0.97 ng/mL). Hyper-reactio luteinalis (HL) was suspected, and we planned to conservatively manage her. Serial ultrasonography of the ovaries showed no change in size, which bilaterally ranged from 80 to 129 mm.

At the 34th week, she discontinued levothyroxine because her TSH level remained low (0.092 µIU/mL); she remained euthyroid until and after delivery. The remaining course of her pregnancy was unremarkable, and she delivered a 2652-g healthy, female neonate at the 39th week via spontaneous vaginal delivery. The neonate's thyroid function was within normal range, with no apparent virilization.



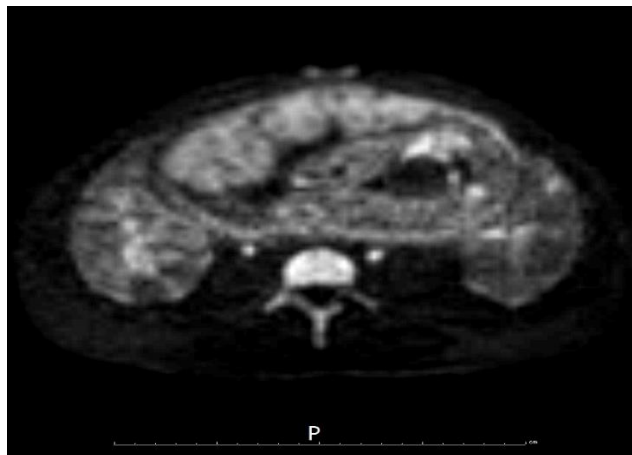
**Figure 2: High-signal-intensity cysts surrounded by moderate-signal-intensity septae in a T2-weighted image.**



**Figure 3: Septae showing low signal intensity in a T1-weighted image.**

Postpartum hormonal levels were assessed, and showed rapidly decreasing testosterone and hCG. She claimed that her lactation increased after 3 weeks postpartum. The ovaries gradually decreased in size, and right and left ovaries measured 61 and 69 mm, respectively, at 1 month postpartum. Their sizes normalized, and the number of

cysts decreased 2 months postpartum, remaining unchanged thereafter. Histopathological assessment of the placenta was unremarkable.



**Figure 4: Septae showing low-to-iso signal intensity in a diffusion-weighted image.**

## DISCUSSION

HL is a rare benign condition of not-well-understood etiology, with over 51 cases reported so far. It is characterized by bilateral multiseptated cystic masses containing multiple theca lutein cysts, which is frequently caused by overstimulation from hCG.<sup>6</sup> It is usually asymptomatic and is found during the second to third trimester or even incidentally during cesarean delivery or postpartum tubal ligation.<sup>7</sup> HL diagnosis is usually made from the particular pattern of presentation and retrospectively after the sizes of the ovaries return to normal postpartum.

Ultrasonographic findings in the present case were consistent with benign ovarian tumors, in which multilocular cystic masses with septae are characteristic.<sup>8</sup> However, they were not diagnostic because they also had some features of malignancy, where large masses contained solid part and thick septae.<sup>8</sup> Although other malignant features, such as papillary projections larger than 3mm, complex masses, and extratumoral fluid, were not observed in the present case, along with the fact that mass diameters more than 10 cm at the initial diagnosis has a higher risk of malignancy, more detailed evaluation with MRI could be of an acceptable option.<sup>8,9</sup> In MRI, HL may appear as high-intensity cystic masses with intermediate-to-high intensity edematous thickened septal walls on T2-weighted images; septations may have low signal intensity on T1-weighted images, and low signal intensity on diffusion-weighted images. The ADC values may be decreased in some ovarian cancers, whereas unchanged values would likely indicate HL.<sup>10</sup> Furthermore, MRI can depict more distant findings of disseminations or metastases which were not observed in the present case. With the careful evaluation and serial

observation, this patient was successfully managed conservatively.<sup>1</sup>

Surgical management could be of choice when (1) the patient has acute signs and symptoms of torsion and rupture; (2) the mass is complex and malignancy is suspected; and (3) large adnexal masses poses high risk of these complications, and is often planned in the second trimester.<sup>1</sup> During pregnancy, most torsions are reported to occur when the tumor size is between 5 to 10 cm, and the gestational week is between 10th to 17th.<sup>1,9</sup> Although rare, torsion can occur even in the third trimester or when the mass size exceeds 10 cm.<sup>11</sup> In the current case, the patient was referred to our hospital at the gestational age of 30th week, which partly made it difficult to proceed to surgery but also enabled careful evaluation and observation.

Although approximately 30% of HL is associated with elevated androgen levels, only one case of virilized female infant has been reported so far.<sup>12,13</sup> As virilization had been previously reported also in a neonate born from a mother with luteoma, the morphological assessment of the neonate in our case was carefully repeated but no virilizing features were noted.<sup>14</sup> A TSH-like secondary effect of hCG may cause thyroid dysfunction, as observed in the present case. The current case showed the typical clinical HL presentation of enlarging bilateral ovaries in the third trimester with increased hCG and testosterone, with an initially depressed thyroid function that improved with the rise in hCG levels. Although ADC values were not measured in this case, ovarian morphology and signal intensity in diffusion-weighted images assisted in differential diagnosis against malignant ovarian tumors, which helped avoiding unnecessary surgeries. Luckily, the present case underwent otherwise uncomplicated pregnancy and delivery course thereafter. The ovaries normalized postpartum. Surprisingly, thyroid function remained normal without oral supplementation even after hCG became undetectable.

## CONCLUSION

HL is a rare condition complicating pregnancy and is frequently confused with malignant entities. Our case demonstrated the importance of recognizing this disease entity. By careful assessment, HL can be conservatively managed and invasive intervention can be avoided. Hormonal evaluation and MRI may assist in diagnosis. Thyroid function may improve due to hyperstimulation by hCG. Thus, careful monitoring is necessary to avoid hyperthyroidism or thyroid storm. A thorough hormonal and morphological assessment should be performed in the neonate born from a mother with HL.

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*Ethical approval: The study was approved by the Institutional Review Board and the Ethics Committee of the Osaka University Hospital (approval#15240, approved on September 10, 2015) and written permission from the patient has been obtained and patient anonymity is preserved*

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