

# Quadruplet pregnancy complicated by ovarian hyperstimulation syndrome with spontaneous ovulation

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## Summary

Ovarian hyperstimulation syndrome (OHSS) commonly occurs as a complication of ovarian stimulation with gonadotrophins. Spontaneous OHSS is an extremely rare event, but can occur as a result of stimulation with pregnancy-derived hCG. We herein report a case of quadruplet pregnancy complicated by OHSS with spontaneous ovulation. The patient had previously undergone ovarian stimulation with clomiphene citrate plus FSH. After that, she conceived spontaneously and developed OHSS after three weeks of amenorrhea. The OHSS was managed by conservative treatment and improved at six weeks of gestation. However, a quadruplet pregnancy became apparent on ultrasound examination. The patient therefore elected to have an induced abortion. Besides the conception in the cycle without administration of exogenous gonadotrophins, the symptoms in this case had the same kinetics as iatrogenic OHSS caused by ovarian stimulation.

**Key words:** Ovarian hyperstimulation syndrome; Quadruplet pregnancy; Ovulation induction; Spontaneous ovulation.

## Introduction

Ovarian hyperstimulation syndrome (OHSS) is a potentially life-threatening complication. OHSS occurs as a result of excessive ovarian stimulation, typically as a result of ovarian stimulation with gonadotrophins. However, OHSS also has been reported to occur in spontaneous pregnancies [1-3]. In this paper, a case of quadruplet pregnancy complicated by ovarian hyperstimulation syndrome is reported. The patient conceived after spontaneous ovulation. However, she had previously undergone ovarian stimulation. This case is uncommon and interesting with regard to the kinetics of the symptoms.

## Case Report

A 32-year-old female, gravida 1 para 1, was referred to another clinic because of secondary infertility on December 2, 2010. Her past obstetrical and familial histories were unremarkable. She had an ovulatory disorder, but her hormonal testing was normal. She had been receiving ovarian stimulation using clomiphene citrate (CC) and FSH. The last administration of CC started on February 12, 2011, on day 5 of her menstrual cycle, and a 150 IU FSH injection was administered on days 8 and 10 of the cycle. The development of two follicles was detected on ultrasound (US) examination. She was followed up without hCG injection. Her basal body temperature (BBT) continued to be low. After that, menstruation began on March 14. She visited that clinic again due to a complaint of abdominal discomfort on May 2. Her urinary pregnancy test was positive. Her last menstrual period was from April 1 to April 6. Ovulation was estimated to have occurred on April 20 based on the BBT (Figure 1). US examination showed enlarged ovaries and ascites. Moreover, hemoconcentration (hct 45.0%, hgb 15.3 g/dl) was noted on laboratory tests. She was suspected of having OHSS. She consulted our hospital on May 3, and was admitted

on May 5. On admission, she had severe abdominal pain and discomfort. Her body weight had increased 4 kg during a period of three days. US examination showed enlarged bilateral ovaries (right ovary, 79 mm; left ovary, 70 mm) (Figure 2) and massive ascites (Figure 3). Laboratory testing showed hct of 38.4% and hgb of 13.0 g/dl. Hypoproteinemia was noted (total plasma protein 5.2 g/dl and albumin 2.9 g/dl). Her thyroid-stimulating hormone and free T<sub>4</sub> levels were normal (3.6 uIU/ml and 0.82 ng/dl, respectively). CA125 was elevated (363.6 U/ml). CA19-9 and CEA were normal (11.6 U/ml and 0.4 ng/ml, respectively). The serum LH and FSH levels were both < 0.1 mIU/ml. The serum estradiol level was 2759.8 pg/ml. The urinary hCG level was 114.2 mIU/ml on the day of admission and 693.0 mIU/ml two days later. Intravenous fluids were administered to maintain a fluid balance and prevent hemoconcentration. On May 9, her complaints of abdominal pain and discomfort were decreased. On May 18, at six weeks of gestation, she was discharged from our hospital. At this time, four intrauterine gestational sacs were found on US examination (Figure 4). On May 24, at six weeks and six days of gestation, a fetus with a heart beat was detected in each of the four gestational sacs on US examination. The patient requested an induced abortion. After obtaining informed consent, the operation (dilatation and curettage) was performed on June 2. Her postoperative course was uneventful. Bilateral ovaries were normalized on June 24.

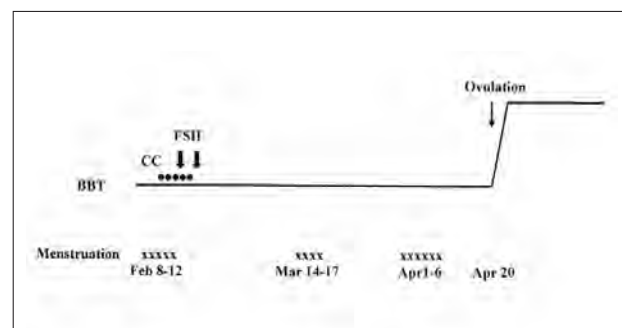


Figure 1. — Menstrual cycle and ovarian stimulation.

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Fig. 2a

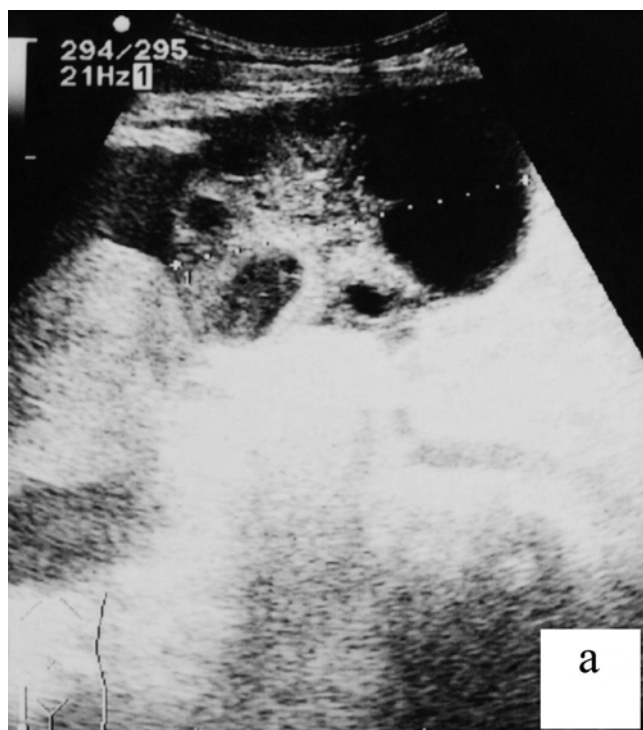


Fig. 2b

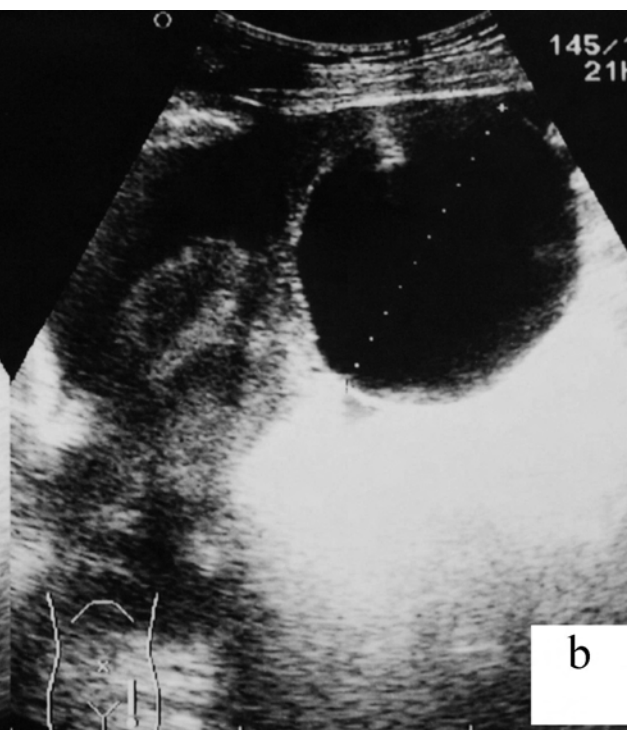


Fig. 3



Figure 2. — Ultrasound image of the enlarged ovaries on the day of admittance to hospital. (a) Right ovary; (b) Left ovary.

Figure 3. — Ultrasound image with the ascites on the day of hospital admittance.

## Discussion

OHSS is a disease characterized by massive ovarian enlargement together with a fluid shift into extravascular compartments. The development of ascites, hypovolemia, oliguria, and thromboembolism occur as a result of the hemoconcentration and coagulation disturbance. This condition is typically seen as a complication of pharmacological ovarian stimulation.

On the other hand, spontaneous OHSS has been reported to be associated with a mutation in the FSH receptor gene [4], hypothyroidism [5], and hydatidiform moles with abnormally high hCG values [6].

Delbaere *et al.* [7] have described the differences of chronology between iatrogenic and spontaneous OHSS. The development of OHSS is thought to be related to hCG, with exogenous hCG inducing ovulation in iatrogenic OHSS or endogenous pregnancy-derived hCG in

spontaneous OHSS. The follicular recruitment and enlargement occur during ovarian stimulation with exogenous FSH in iatrogenic OHSS. Iatrogenic OHSS has been reported to usually develop at between three and five weeks of amenorrhea and then it starts to improve after six weeks of pregnancy [7]. On the other hand, the follicular recruitment and enlargement by pregnancy-derived hCG has been reported to start at between six and ten weeks of amenorrhea in patients with spontaneous OHSS [7]. The hCG level usually peaks between eight and ten weeks of pregnancy. The development of spontaneous OHSS is therefore expected to occur at between eight and 12 weeks of amenorrhea [7].

In this case, ovarian stimulation has been previously performed using CC plus FSH. However, the patient conceived after spontaneous ovulation. Her symptoms of OHSS appeared after three weeks of amenorrhea and improved at six weeks of gestation. Besides the concep-

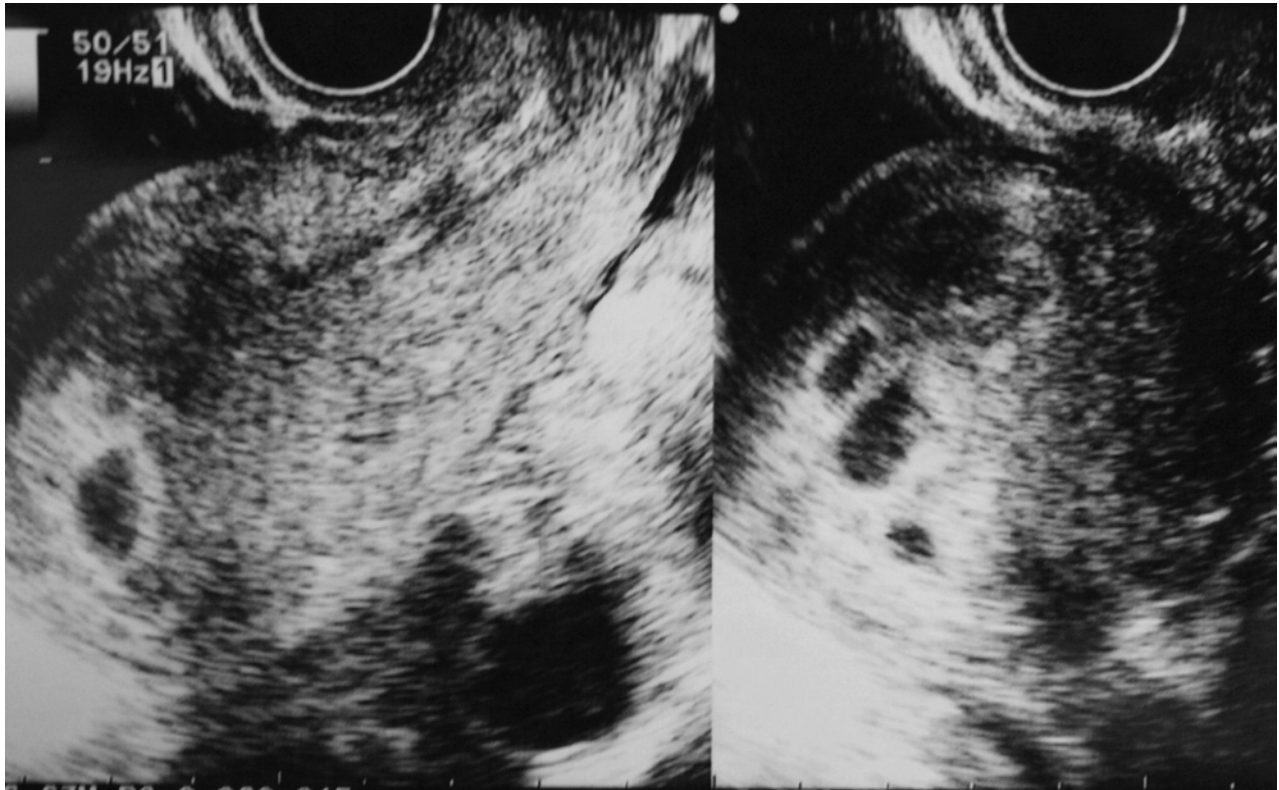


Figure 4. — Ultrasound image showing four gestational sacs in the uterus.

tion in the cycle without the administration of exogenous gonadotrophins, the symptoms had the same kinetics as that of iatrogenic OHSS. This case is uncommon and interesting with regard to the kinetics of the symptoms. The correlation between previous administration of CC plus FSH and the development of symptoms are uncertain.

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