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Case Report

Development and management of ovarian hyperstimulation syndrome in spontaneous singleton pregnancy

Sercan Kantarcı^{1*}, Yaşam Kemal Akpak¹, Betül Öztürk¹, Serkan Oral², Atakan Emre¹, Alper İleri¹, Adnan Budak¹, Gökhan Tosun¹, Hamdi İnan¹, Mehmet Özeren¹

¹Department of Obstetrics and Gynaecology, Tepecik Training and Research Hospital, Izmir, Turkey

²Department of Obstetrics and Gynaecology, Halic University, Istanbul, Turkey

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***Correspondence:**

Dr. Sercan Kantarcı,

E-mail: sercan.kntrc@gmail.com

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ABSTRACT

Ovarian hyperstimulation syndrome (OHSS) is one of the most life-threatening complications of ovulation induction. However, rarely, OHSS can develop spontaneously during pregnancy without induction of ovulation. It has been shown in the literature that some diseases such as polycystic ovary syndrome (PCOS), hypothyroidism, and pituitary adenoma may accompany spontaneous OHSS. Spontaneous OHSS should be included in the differential diagnosis in first-trimester pregnancies with nausea, vomiting, and acute abdomen. The focus should be on preventing possible complications and initiating early treatment immediately after diagnosis.

Keywords: Spontaneous ovarian hyperstimulation syndrome, Ovarian torsion, Pregnancy first trimester complications, Ovarian cysts, Ovulation induction

INTRODUCTION

Ovarian hyperstimulation syndrome (OHSS) usually occurs in approximately 10% of cases due to ovulation induction.¹ Although spontaneous OHSS is very rare, it has a later onset than iatrogenic OHSS. Although spontaneous OHSS is generally seen between 8-14 weeks, its etiopathogenesis has not been determined clearly.²

However, spontaneous OHSS can rarely occur due to the overstimulation of FSH receptors via glycoproteins such as FSH, LH, TSH, and hCG.³ Common risk factors are being younger than 35 years of age, low body mass index (BMI), a history of PCOS, and a previous history of OHSS.⁴ Spontaneous OHSS may have complications secondary to hemoconcentration and electrolyte imbalance.⁵ Iatrogenic OHSS is classified as mild, moderate, severe, and critical according to ultrasound and laboratory tests. Severe-critical OHSS may present severe

clinical conditions such as acute renal failure, massive hydrothorax pericardial effusion, ARDS. While conservative treatments are preferred in managing patients who develop spontaneous OHSS, medical and surgical treatment options are also available depending on the severity and type of symptoms.⁶

CASE REPORT

An 18-year-old Turkish-origin primigravid spontaneous patient was referred to our center from an external center with complaints of persistent abdominal pain, bloating, dyspnea, nausea, and vomiting. The age of the first menstrual period is 14 and her periods are regular. The patient, who has no known comorbidity, history of drug use, and previous operation, is in the 10th week of spontaneous pregnancy without using an ovulation induction agent, according to the last menstrual period. The patient's height was 155 cm, her weight was 59.3

(body mass index: 24.6), and her abdominal circumference was 86.5 cm. The ovaries were evaluated as normal in the pre-pregnancy ultrasound. The abdomen was distended in the patient's physical examination, bowel sounds, lung sounds, and heart sounds were evaluated as normal. In transabdominal ultrasound, the single intrauterine fetus was compatible with ten weeks according to Crown-rump length (CRL), fetal heart rate was positive (126 fhr), the bilateral multiloculated right ovary was 125 x 90 x 127 mm in size, while left ovary was 125 x 81 x 103 mm. The dimensions of both ovaries increased significantly, and the upper border of the ovary ended at the level of the umbilicus. While diffuse free fluid was observed in all quadrants, no signs of torsion were found on Doppler ultrasound. In the cardiac echo examination after the cardiology consultation, pericardial effusion was not observed, while the ejection fraction (EF) was 65% and reported as normal echo findings. Laboratory results are Hb:13.5 Htc:40.3 Beta hCG:201477, TSH:1.54, sT3:2.53, sT4:0.95, WBC:11,800, PLT:404,000, Na:130 mmol/l, Ca:8.47 mg/dl, K:3.9 mmol/l, Cr:0.7 mg/dl, Albumin:2.98 g/dl, and liver enzymes were found to be moderately high. As the tumor markers were CA125:129.7 U/ml, the patient was hospitalized, and a gynecological oncology consultation was requested. Since gynecological malignancy was not considered in the consultation, follow-up continued in our clinic for further examination and treatment.

The patient was evaluated as moderate OHSS. By monitoring the patient's intake and output, daily 1500 cc NaCl infusion plus Voluven 500 cc infusion so 2 liters IV infusion, ceftriaxone 1*2 gr IV, prophylactic 0.4 cc SC low-molecular-weight heparin (LMWH) and, if needed, 500 mg paracetamol IV infusion treatment were arranged. Recent intake and output, waist and abdominal circumference, weight, and fluid electrolyte levels were monitored. After the prophylactic LMWH treatment in the patient with normal coagulation test results, nosebleeds and no hemoconcentration were observed, so LMWH treatment was stopped. After ten days, the patient's clinical and laboratory values and intake-output balance tended to return to normal, and she was discharged to be called for control one week later. The patient came to her first control one week later. The ovary dimensions of the patient who did not have any active complaints were seen to have decreased by 70*85 mm and the left ovary by 79*90 mm. Abdominal distension was decreased, free fluid was at the physiological level, and laboratory values were consistent with the week of gestation.

In the subsequent follow-ups, the double screening test was found to be low risk. The 2nd-trimester anomaly scan was normal. The patient's routine pregnancy follow-up, who also came regularly for subsequent pregnancy follow-ups, was normal, and she delivered a 3200 g live male baby with 9 APGAR by normal spontaneous vaginal delivery at 39 weeks. All findings and imaging were within normal limits in the ultrasonography and laboratory evaluations performed at the 6th week of postpartum.

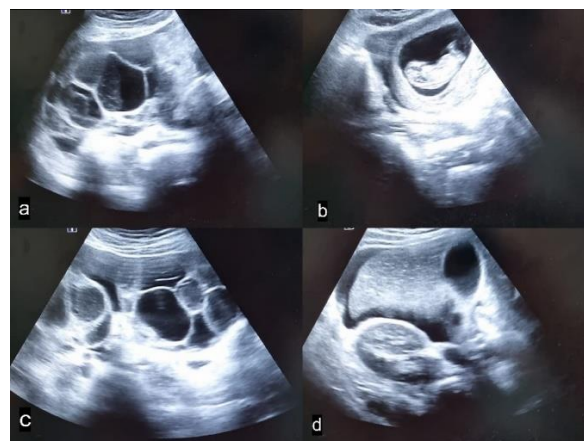


Figure 1: (a) Multiloculated 125x90x127 mm right ovary, (b) diffuse free fluid around the uterus (CRL 10W), (c) bilateral multiloculated big kissing ovary, (d) diffuse fluid in Morison's pouch.

DISCUSSION

Although spontaneous OHSS is usually seen between 8 and 14 weeks, in our case, it was diagnosed at an external center at the 10th week and referred to us. Although spontaneous OHSS is very rare, its pathophysiology has not yet been fully elucidated, but VEGF and VEGFR in the granulosa cells of the corpus luteum play a critical role in the development of OHSS. In addition, hCG and gonadotropins increase the amount of VEGF.⁷ Vasoactive substances secreted by the ovaries increase mesothelial hyperpermeability and cause fluid leakage from the intravascular space to the third space. hCG, estradiol, prolactin, histamine, and prostaglandins are mediators that aggravate OHSS. However, vasoactive substances secreted by the ovary, such as TNF- α , endothelin-1, and VEGF, which are better known today, increase vascular permeability.^{8,9} According to the De Leener classification, spontaneous OHSS consists of 3 types. Type 1 can cause recurrent OHSS associated with FSH receptor polymorphism. Type 2 is the most common type, hydatidiform mole accompanied by high hCG, and the type seen in multiple pregnancies. Type 3 is associated with hypothyroidism.¹⁰ Cases are primarily seen in patients with multiple pregnancies accompanied by high hCG levels, hydatidiform moles, or hypothyroidism characterized by high TSH levels. According to the literature, primary hypothyroidism characterized by high TSH levels or a very rare TSH-secreting adenoma may be associated with spontaneous OHSS.² In our case, the beta hCG: 201477 value of the patient was higher than the week of gestation, but the thyroid hormones TSH:1.54 sT3:2.53 sT4:0.95 were found to be normal. Although our case did not have a history of hydatidiform mole, an appearance compatible with a mole was not observed on ultrasound. In addition, the postpartum placenta was sent to pathology and reported as a placenta compatible with its normal week.

Known risk factors for OHSS are young age, low BMI, polycystic ovary syndrome, high-dose gonadotropin use, rapidly rising estradiol level, and a history of the previous OHSS. There are cases of spontaneous OHSS described in patients with polycystic ovary syndrome.¹¹ Our patient had regular menstrual periods before pregnancy, no history of hair growth, and both ovaries were found to be normal on ultrasound.

Malignancy should also be considered in ovarian cysts that grow rapidly in a short time. Germ cell tumors should be considered in bilateral ovarian masses in adolescent pregnant women.¹² In addition, CA125:129.7 was found in our patient. In Doppler ultrasound findings, ovarian cysts were evaluated as benign cystic because of the absence of solid components and their benign appearance of blood supply. In addition, malignancy was ruled out by requesting a gynecological oncology consultation. In addition, pregnancy luteoma and hyperreactio luteinalis (HL) can be considered in the differential diagnosis of OHSS. Pregnancy luteoma is a non-neoplastic solid ovarian mass lesion caused by excessive androgen secretion by the ovary, generally asymptomatic, seen in the last trimester and regressed with delivery. HL is a rare condition with bilateral multiloculated ovarian cysts that typically appear in the last trimester of pregnancy and regress with delivery.¹³

Ovarian torsion is a true gynecological emergency. Although it is seen in approximately 3% of all gynecological emergencies, 12-25% of these cases are pregnant.¹⁴ It usually presents with acute unilateral pain, accompanied by nausea, vomiting, defense, and rebound. Laparoscopy is one of the preferred approaches in adnexal torsion. Laparoscopy can be safely performed during pregnancy, especially in the early second trimester. In our case, we evaluated the ovarian blood supply with daily Doppler USG and excluded ovarian torsion and ovarian cyst rupture with the daily physical examination.

In the clinical presentation of OHSS, ascites, pleural effusion, and edema are observed due to fluid loss to the third space. It is this fluid loss that mainly causes mortality and morbidity. Hypovolemia due to fluid and protein loss, and the most severe complications related to hemoconcentration are hypercoagulability and decreased renal perfusion.¹⁵ Vital organs and systems can be severely damaged in critical OHSS. Acute renal failure, cardiac arrhythmia, respiratory failure, disseminated intravascular coagulation (venous and arterial thrombosis), and anuria can result in death. The pleural effusion transforms into massive hydrothorax with pericardial effusion. Sepsis and acute respiratory distress syndrome (ARDS) can further complicate the clinical picture. For this reason, as in our case, close monitoring of vital and fluid balance, albumin level, use of LMWH are critically important for the follow-up and prevention of OHSS complications.

Spontaneous OHSS is a very rare condition. A delay in diagnosis can lead to life-threatening complications.

Although there is no specific treatment, most cases require hospitalization. Hemodynamic close monitoring, intravenous albumin, crystalloid infusion, and thromboembolism prophylaxis constitute the basic treatment principles.¹¹ OHSS should be considered in the differential diagnosis of patients with first-trimester nausea, vomiting, edema, abdominal distension, increased ovarian size, who did not receive ovulation induction, and should be followed closely for possible complications.

CONCLUSION

In our case, increased ovarian size, abdominal pain, bloating, nausea, vomiting and ascites were detected on ultrasound. Although she did not receive ovulation induction, she was thought to be clinically compatible with OHSS. She was followed closely for complications of ovarian torsion, electrolyte imbalance, pulmonary edema, renal failure, deep vein thrombosis. Fluid therapy was arranged according to the fluid intake and output, and anticoagulant therapy was started. It should be kept in mind that OHSS can also develop spontaneously. The importance of early diagnosis and treatment should be emphasized in terms of preventing life-threatening complications.

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