Spontaneous Ovarian Hyperstimulation Syndrome in Second Pregnancy of a Healthy Pregnant Woman

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Abstract- Spontaneous ovarian hyperstimulation syndrome (OHSS) is an uncommon type of OHSS that is characterized by gastrointestinal symptoms and complications of accommodation of body fluids in third spaces in the absence of medical ovarian stimulations. This syndrome is mostly seen in multiple or molar pregnancies with an underlying medical condition such as hypothyroidism. Treatment of spontaneous OHSS depends on the patient's clinical condition. Appropriate management will warrant a successful pregnancy. The aim of this report is to introduce a case of spontaneous ovarian hyperstimulation syndrome in second pregnancy of a healthy pregnant woman. The patient was a 8 weeks pregnant female who referred to gynecology and obstetrics clinic because of gradual abdominal distension, abdominal pain and nausea from one month ago. The patient didn't have any history of the specific predisposing factors of OHSS such as thyroid gland dysfunction or multiple pregnancies. Abdominal sonography showed enlarged ovaries with prominent follecules as well as free fluid in the entire abdomen. Elevated levels of HCG (312850 mlU/ml) and carcinoembryonic antigen (106 U/ml) were the remarkable laboratory findings. We successfully controlled the patient by conservative management and the size of ovaries returned back to normal by 17th weeks of gestation. On sonographic follow-ups, untill delivery, the patient was symptom-free and a healthy infant was born. While spontaneous OHSS is a rare and life-threatening condition, conservative management including albumin and anticoagulant administration as well as paracentesis of body third space fluids, will be a promising approach in the stable patients.

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Introduction

Ovarian hyperstimulation syndrome (OHSS) is an uncommon and potentially life-threatening medical event (1). OHSS is defined as acute third space fluid sequestration and ovarian enlargement in early pregnancy (2). This syndrome may be encountered during controlled ovarian stimulation which is employed in attempt to retrieve more oocytes for assisted reproductive techniques (1). However, spontaneous OHSS during pregnancy is extremely rare. There are various etiologies and the exact cause is unknown (3). While the most probable cause is a mutation in follicular stimulating hormone (FSH) gene, hypothyroidism, molar or multiple pregnancies are mostly seen with spontaneous OHSS (3-5). Despite laboratory tests such as thyroid function tests, human chorionic gonadotropin (HCG) and CA-125 antigen, ultrasound studies are mandatory for determining both diagnosis and differential diagnosis (3,6). After confirming the diagnosis, prompt management by even conservative or invasive management should be considered. Despite ovarian torsion or unstable conditions, conservative management is preferred in most cases (7). In this report, we present a case of spontaneous OHSS with normal laboratory level of thyroid function tests and singleton pregnancy that was successfully managed using conservative methods.

Case Report

A 20-year-old Caucasian female (G: 2, P: 1) at 8th weeks of pregnant referred to gynecology and obstetrics

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clinic because of gradual abdominal distension, abdominal pain and nausea from one month ago. The pain was consistent with moderate intensity and localized over the hypogastric area without any radiation. The patient did not have previous medical or surgical history and didn't receive any medication. Vital signs were as follows: pulse rate: 110 beat/minute, breath rate: 22 bpm, systolic/diastolic blood pressure: 110/70 mmHg and axillary temperature: 37° C. During the examination, the abdomen was distended and ascites was prominent. Ultrasound revealed a pregnancy sac with a live 8 weeks fetus located in the uterus. The size of both ovaries was bigger than normal (Right ovary: 80*75 mm and Left ovary: 90*75 mm) containing multiple follicles. Free fluid was prominent in the abdominal cavity. Laboratory test results were as follows: blood cell count: 10000×10^9/L, Platelet count: 25300×10^9/L, hematocrit: 38%. Also, thyroid function tests were normal and elevated HCG level (312850 mIU/ml) was noticed. CA-125 level was 106 U/ml and other laboratory results were unremarkable. According to physical and laboratory findings, the possible diagnosis was moderate OHSS. The patient received Ampule chlorpheniramine (10 mg tid) and acetaminophen suppository (325 mg) three times daily. Also, serum and fluid intake was restricted. Serum electrolytes and patient's input and output, weight and waist circumference were measured daily. In the hospital, the patient developed dyspnea, oliguria and increase in hematocrit and waist circumference. In the next ultrasound which was performed 3days later, abdominal ascites and ovary size were increased (Left ovary: 125*80 mm and right ovary: 135*75 mm). Also, pleural effusion was prominent. Low molecular weight heparin (40 mg daily subcutaneously) and serum albumin (20% intravenously) was administered. Ascites fluid paracentesis was performed two times during admission. The symptoms reduced after paracentesis as the previous treatment strategy was continued. At 11th week of gestation, as the abdominal pain and dyspnea were diminished, the patient was discharged and underwent routine follow up. The size of both ovaries become normal at 17th weeks of gestation. According to previous history of cesarean section and initiation of uterine contractures, cesarean section was performed at gestation age of 38 week. The size of both ovaries was approximately 40*60 mm with multiple follicles at each site. A healthy boy weighing 3200 gr was born with first and fifth minutes Apgar score of 9 and 10. Right and left ovary were 27*52 mm and 31*53 mm, respectively, resembling polycystic ovary appearance 6 weeks after cesarean section. The patient was symptom-free with normal menstrual cycles until post-cesarean section 6 months of follow up. CA-125 level decreased to normal limit (18.5 U/ml, normal range: up to 35 U/ml).

Discussion

Spontaneous OHSS during pregnancy is a rare event. Most of the reported cases are multiple or molar pregnancies and related to thyroid gland disorders. Spontaneous OHSS in singleton pregnancy is extremely rare and can be managed promptly by conservative approach.

Spontaneous OHSS usually starts from 8 weeks of amenorrhea (3). Diagnosis of spontaneous OHSS can be easily made by typical symptoms including nausea, vomiting, abdominal pain and distention in pregnant women without ovarian stimulation (6). Ultrasound study of ovaries is the next step in patients with a suspicious diagnosis of OHSS. As in our patient, multicystic ovaries are detectable in both ultrasound and magnetic resonance studies (3,6). Imaging modalities are also useful in rolling out important differential diagnosis such as ovarian tumors (6). Also, laboratory tumor markers which are specific for ovarian and abdominal tumors will be useful for eliminating different diagnosis. However, some tumor markers such as CA-125 may provide confusing results in spontaneous OHSS patients. CA-125 levels increase in several benign conditions such as hypothyroidism, irritation of peritoneum, pleura, and pericardium are also reported to be related to ovarian volume (5,8). Similar to our patient, Kanza *et al*., reported a case of spontaneous OHSS with an elevated level of CA-125 that was associated with primary hypothyroidism (5). In our case, level of CA-125 marker decreased to normal 6 mounts after discharge.

The main etiology behind spontaneous OHSS is still unknown. However, activation of suppressor of cytokine signaling and dysregulation of IL-2 expression in response to HCG is commonly considered to be responsible for OHSS (2). High HCG and thyroid-stimulating hormone (TSH) concentration will play an important role in ovarian stimulation. These situations are seen in the molar or multiple pregnancies and hypothyroidism (3). However, in some cases such as the current case, none of these etiologies were present. Cabar *et al*., reported a similar case of spontaneous OHSS in a nulliparous woman which was not related to any of these etiologies (7). They have suggested FSH gene mutation as the most likely cause of OHSS. They stated that identifying the mutation will be helpful in predicting the recurrence rate in later pregnancies (7). However, our

case had the history of a healthy child with an uneventful pregnancy and OHSS developed for the first time in her second pregnancy. The present case is similar to the case reported by Dieterich *et al*., (4). They reported a patient with 2 episodes of spontaneous OHSS and 2 different side diagnosis in a patient with FSH receptor mutation. The elevated androgen and HCG concentration in the first pregnancy led to OHSS and abortion (4). Normal HCG level and hypothyroidism despite OHSS in the next pregnancy resulted in successful delivery (4). In this report, our patient was not evaluated for the possibility of mutations in the FSH receptor gene.

After a diagnosis of spontaneous OHSS, appropriate treatment will be the next clinical challenge. Some researchers have provided classification and treatment guidelines (3). Panagiotopoulou *et al*., provided a flow chart for better classification of OHSS (6). According to this chart, due to high level of HCG and normal level of TSH, LH, and FSH, the most probable type of OHSS in our case was Type II. Conservative management is recommended in patients with stable hemodynamic status. Intravenous albumin infusion and drainage of pleural or peritoneal fluid will improve the patient's symptoms (3). Our patient responded to conservative treatment and ascites fluid drainage. Caber *et al*., reported a similar case with normal levels of TSH and HCG that was successfully treated with intravenous albumin, furosemide and enoxaparin (7).

While spontaneous OHSS, despite multiple or molar pregnancy and hypothyroidism, is a rare and life-threatening condition, conservative management including albumin and anticoagulant administration as well as paracentesis of body third space fluids will be a promising approach in stable patients.

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