Received: 20.11.2014 - Accepted: 15.01.2015

A CASE OF OVARIAN HYPERSTIMULATION SYNDROME IN A PATIENT WITH POLYCYSTIC OVARIAN SYNDROME

Tuğba Gül[1], Vedat Uğurel[2]

[1]Trakya University School of Medicine, Edirne, TURKEY
[2]Trakya University School of Medicine, Department of Obstetrics and Gynecology, Center for Assisted Reproductive Technology, Edirne, TURKEY

ABSTRACT

Aims: The most common and the most dramatic complication of ovulation induction is overian hyperstimulation syndrome. The syndrome has a wide range of clinical manifestations ranging from mild ascites to life-threatening conditions. In this case report, it is aimed to examine a patient with polycystic ovarian syndrome who was hospitalized with pulmonary symptoms and widespread ascites in abdominal cavity developed due to ovarian hyperstimulation syndrome.

Case Report: After ovulation induction, intrauterine insemination (IUI) was performed on the 26 year-old patient with the history of primer infertility, hypothyroidism, polycystic ovarian syndrome for 4 years. Ten days after IUI, the patient applied to our clinics with abdominal distention, dyspnea, cough, nausea, vomiting and was admitted to our Obstetrics and Gynecology Clinic. The patient developed plevral effusion and diagnosed with Grade-4 Ovarian Hyperstimulation Syndrome is presented in this case report.

Conclusion: Ovulation induction and intrauterine insemination are the most frequently used assisted reproductive methods that cause Ovarian Hyperstimulation Syndrome (OHSS). The patients with Polycystic Ovarian Syndrome (OHSS), hypothyroidism and multiple follicles should be closely monitored and hospitalized early to drain ascites on time if needed.

Key Words: Policystic Overian Syndrome, prevral Effusion, hypothyrodism, cabergolin

INTRODUCTION

Overian Hyperstimulation Syndrome (OHSS) is a serious, life-threatening clinical case which manifests itself with multiple luteal and hemorrhagic cysts in ovaries and massive ovarian growth. It might happen spontenaously but it mostly happens iatrogenicaly, because of ovulation induction or controlled overian hyperstimulation. Symptoms such as hemoconcentrantion, thromboembolism tendency, fluid and electrolyte imbalance, ascites, weight gain, oliguria, pleural/pericardial effusion might accompany. Incidence of OHSS is between 1-10% when severe OHSS is less than 2% (1). As moderate OHSS is seen 15.4% in Polycystic Overian Syndrome (PCOS), rare spontaneous cases have also been reported (2). Even though there are no certain information on its pathogenesis, increased capillary permeability in ovaries and peritoneal cavity is thought to be the reason (3).

In this case report, it is aimed to present the patient with a medical history of PCOS and hypothyroidism that showed OHSS symptoms after ovulation induction.

CASE REPORT

For a total of 15 days, the 26 year-old patient with 4 years history of primer infertility, hypothyroidism, polycystic ovarian syndrome was applied 6500 IU rHCG (recombinant human chorionic gonadotrophin) to trigger ovulation after stimulation with 1550 IU FSH (follicle stimulating hormone). Two follicules sized 15.5 mm and 15 mm in the right ovary and multiple folliculeles, the largest being 12 mm in left ovary have developed. Intrauterine insemination (IUI) has been performed on the patient who had an endometrial thickness of 12 mm. Ten days after the IUI, the patient applied to our clinic

Adress for Correspondence: Tuğba Gül,Trakya University School of Medicine, Edirne, TURKEY - e-mail: drtugbagul@hotmail.com

with abdominal distention, dyspnea, cough, nausea, vomiting and was admitted to our Obstetrics and Gynecology Clinic. Generalized ascites in the abdominal cavity has been detected with transabdominal ultrasonography (USG). Right ovary was 8x9 cm and left ovary was 11x8.8 cm. Pulmonary diseases consultation has been requested considering the patient's dyspnae and cough. Although respiratory sounds were found to be decreased bilaterally in bases, neither rales nor rhonchi were detected. Effusion was also detected in lung bases. All the symptoms have been thought to be secondary to generalized ascites in the abdominal cavity. Cardiology consultation revealed normal S1 and S2 sounds and no additional sounds or murmur. Pulmonary and cardiac pathologies were ruled out after pulmonology and cardiology consultations. After ortopnea and dyspnea symptoms got worse, 2 liters of fluid were extracted from the Pouch of Douglas with transvaginal ultrasound guidance. There were no bleeding or other complications. Dyspnea got better dramatically. Patient's lab results have been found as follows: Hb 14.6 g/dL, Htc 41.7%, leukocyte count 22.5x103 /uL, neutrophil count 14x103 /uL, lymphocyte count 5.67x103/uL, total serum protein 5.3 g/dL, LDH 121 U/L, ALP 32 U/L, GGT 14 U/L, ALT 14 U/L, AST 18 U/L, uric asid 6.6 mg/dL, urea 15 mg/dL, creatinine 0.57mg/dL, prothrombine time 13.3 s, prothrombine activity %97, INR 1.02, APTT 27.4 s. Serum electrolyte values were as follows: Na 138 mmol/L, K 5 mmol/L, Cl 113 mmol/L, Ca 8.7 mg/dL. Beta-HCG values in 2nd, 5th, 6th, 9th and 12th days were 46.93, 110.07, 137.81, 337.91, 1155.22 mIU/ml, respectively. Permanent tunneled peritoneal drainage catheter was implanted on the 4th day of admission by interventional radiology to manage increased ascites. Total serum protein, albumin, urea and creatinine in urine and Hb, Htc were measured by recording intake and output of fluid. The patient was given enoxaparine, acetylsalicylic acid, paracetamol, cabergoline. Considering intake and output of the fluid, 500 mL 6% Hydroxyethyl starch solution and 1000 mL 0.9% NaCl were given as supportive care. Since her albumin level was 2.4 g/dL on the 3rd day of follow-up, she started to receive 100 mL 20% human serum albumin which was continued for 20 days. Transvaginal ultrasound revealed fetal heartbeats in 3 different gestational sacs 2 weeks after her admission. According to endocrinology consultation, thyroid was non-palpable and lab results were as follows: T3 2.39 pg/mL, T4 0.65 ng/mL, TSH 13 mIU/mL. Levotroxin was planned as 50 mg for 5 days and 75 mg for 2 days. Patient was discharged on 26th day based on the following lab results: Hb 12.1 g/dL, Htc 35.8%, total serum protein 5.5 g/dL, albumin 3.2 g/dL; there was a decrease in ascites volume and patient's general condition was fine. The outpatient's permanent drainage catheter was not removed and her intake and output of fluid were monitored. On the 10th day after the discharge, transabdominal USG revealed twin pregnancy with CRL (Crown rump length) compatible with 9 weeks+1day and 7 weeks+1day, respectively. In the third sac no heartbeat was seen. After 2 weeks, in clinical follow-up, a single fetus with a heartbeat and CRL of 3,49 cm was revealed. The patient is currently followed-up as a 26 weeks pregnant.

DISCUSSION

Ovarian hyperstimulation syndrome is one of the severe complications of assisted reproduction.

Although very rarely, OHSS can also occur spontaneously. Even though the exact mechanism of OHSS is still unknown, the increase in capillary permeability is held responsible. Vasoactive agents secreted from growing ovaries trigger OHSS manifestation by increasing capillary permeability. Probable agents increasing the vascular permability are vascular endotelial growth factor (VEGF), renin-angiotensin system components and some cytokines (4).

Risk group for OHSS consists of people who are young, anovulatory infertile with oligomenorrhea, diagnosed with PCOS, have multiple follicles during day 1 hCG, experienced pregnancy formation after ovulation induction, and have hypothyroidism and hyperprolactinemia (1). This case was a 26 year-old patient who was diagnosed with PCOS and hypethyroidism, and developed multiple follicles during hCG administration, followed by pregnancy.

Overian Hyperstimulation Syndrome (OHSS) has two different clinical forms, early and late. Early OHSS is related to the ovarian response to the stimulation and is the acute effect following exogenous hCG administration 9 days later. Late OHSS occurs after 10 days and it is related to endogenous hCG production with embryo implantation and administered supportive hCG for luteal phase more than the ovarian response (5).

Severe OHSS ratio among all ovarian hyperstimulations is 0.5-5%, according to reports (6). Severe OHSS cases are usually late-onset. 68% of severe OHSS cases are late-onset. In addition, studies report that multiple pregnancy ratio is higher in late OHSS cases (7). In this case, the patient had late OHSS and multiple preg-

nancy, as well.

In most cases, OHSS limits itself and after approximately 6-8 weeks disappears spontaneously. On the other hand, there are some fatal cases related to pleural/pericardial effusion, hypervolemia, oliguria, hemorrhage, deep vein thrombosis and pulmonary thromboembolism (8, 9).

There are various classifications to determine OHSS severity. The OHSS classification which is in use today was created by Golan et al. (10):

Table 1: Golan Classification (10).

MILD OHSS	
Grade-1	Abdominal distension and irritaition.
Grade-2	In addition to Grade-1 sypmtoms, also vomiting and/or diarrhea. The size of ovaries are over 5-12 cm.
MODERATE OHSS	
Grade-3	Mild OHSS sypmtoms + Ultrasonographic ascites
SEVERE OHSS	
Grade-4	Moderate OHSS symptoms + clinically ascites and/or hydrothorax symptoms or respiratory problems
Grade-5	In addition to all these symptoms, volume changes, increased blood viscosity (related to hemoconcentration), coagulation anomalies and renal perfusion and function disorders

The patient was diagnosed as OHSS Grade 4, based on Golan classification.

Main treatment of OHSS is supportive. The treatment includes serum replacement to increase intravascular volume, albumin infusion if hypoalbuminemia is detected and thromboembolism prophylaxis. During patient follow-ups fluid, intake and output measurements, blood electrolytes, Hb, HCT, liver and kidney function tests are performed (11). Even the termination of pregnancy act may be necessary , if conservative treatment fails (12).

In the recent years, dopamine agonists are in frequent use for OHSS prophylaxis. The decreasing effect of dopamine agonists on VEGF receptor 2 activity is also reported on animal models (13). In a meta-analysis about the risk of OHSS, which was carried out in 2010 (14), 5 randomised controlled studies were included and OHSS incidence was decreased by approx. 60%, depending on cabergoline usage. Cabergoline is the only agent used as a VEGF agonist in both early and late OHSS, and it is effective at reducing OHSS severity. In this case, during her hospitalisation, the patient was given dopamine agonist cabergoline as 0,5 mg tablet per day.

As in our case, ovulation induction and intrauterine insemination are the most frequently used assisted reproductive methods that cause Ovarian Hyper Stimulation Syndrome. The patients with Polycystic Ovarian Syndrome, hypothyroidism and multiple follicles should be closely monitored and hospitalized early to drain ascites on time if needed.

Ethics Committee Approval: N/A
Informed Consent: Written informed consent was obtained from the participants of this study.
Conflict of Interest: The authors declared no conflict of interest.
Financial Disclosure: The authors declared that this study received no financial support.

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