Severe ovarian hyperstimulation syndrome in spontaneous pregnancy treated successfully with cabergoline

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Abstract

Ovarian hyperstimulation syndrome (OHSS) is a relatively common complication in infertile patients treated with exogenous gonadotropins. Ovarian hyperstimulation in spontaneous pregnancies is a rare but possible. The pathogenesis of spontaneous OHSS is not well known. Risk factors for OHSS are young age, polycystic ovaries, low body mass index, high gonadotropin dose, increased estradiol and human chorionic gonadotropin levels, multiple pregnancy, OHSS history, molar pregnancy and hypothyroidism. In this report we present a case of severe spontaneous OHSS with a brief summary of the literature. She was hospitalized and treated in the clinic with the diagnosis of severe OHSS accompanying spontaneous pregnancy.

Introduction

Ovarian hyperstimulation syndrome is a relatively common iatrogenic complication of ovulation induction and controlled ovarian hyperstimulation induced with exogenous gonadotropins.¹ The incidence of OHSS is about 1-10% and severe OHSS is seen in less than 2% of cases.² Massive ovarian enlargement, multiple cysts, ascites, oliguria, abdominal pain, hemoconcentration, thrombosis, pleural effusion, electrolyte imbalance, renal failure, acute respiratory distress syndrome, hypovolemia and death can accompany severe OHSS.³ OHSS following spontaneous ovulation is very rare. In this report, a case of severe

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OHSS accompanying spontaneous singleton pregnancy is summarized.

**Case Report**

A 27 year-old gravida 3 para 2 woman presented to the clinic with a complaint of abdominal pain, abdominal distension, dyspnea, nausea and vomiting. She previously had two healthy deliveries at term. The medical history was uneventful and no drug use was reported before or during the pregnancy.

Vital signs of the patient were normal. Abdominal distension and bilateral adnexal pain were noted during the physical examination. Transabdominal ultrasonography revealed a 10-week, singleton pregnancy. Both of the ovaries were enlarged and multicystic (Left ovary: 118 x 113 mm, right ovary: 127 x 117) and there were ascites in the abdomen.

Blood tests revealed hemoconcentration (Hb: 16.7 g/dl, Htc: 47.40%, WBC: 25260, PLT: 360000/mm3), hypocalcaemia (7.77 mg/dl), hypoproteinemia (Albumin: 2.2 g/l).

The patient was hospitalized with the diagnosis of severe spontaneous OHSS and treated with intravenous fluid replacement, albumin infusion, and low molecular weight heparin. A specialist performed respiratory physiotherapy. Daily weight and abdominal circumference measurements were performed. Blood tests were also repeated daily and treatment of the patient was managed accordingly.

After the first week of hospitalization, an increase in body weight and abdominal circumference was seen. The patient had dyspnea, and there was bilateral pleural effusion in the chest x-ray and thoracic ultrasonography. Thoracentesis was performed. The fluid was transude in manner and both cytological and microbiological examinations were normal. There was an increase in the ovarian size (left ovary: 176 x 139 mm, right ovary: 166 x 132 mm) (Picture 1, Picture 2). Cabergoline 0.5 mg/day and dexamethasone 0.5 mg/day treatment was started.

**Picture 1. Left Ovary**

Blood tests revealed hemoconcentration (Hb: 16.7 g/dl, Htc: 47.40%, WBC: 25260, PLT: 360000/mm3), hyponatremia (Na: 123 mmol/l), hypocalcaemia (7.77 mg/dl), hypoproteinemia (Albumin: 2.2 g/l).

**Picture 2. Right Ovary**

After the first week of hospitalization, an increase in body weight and abdominal circumference was seen. The patient had dyspnea, and there was bilateral pleural effusion in the chest x-ray and thoracic ultrasonography. Thoracentesis was performed. The fluid was transude in manner and both cytological and microbiological examinations were normal. There was an increase in the ovarian size (left ovary: 176 x 139 mm, right ovary: 166 x 132 mm) (Picture 1, Picture 2). Cabergoline 0.5 mg/day and dexamethasone 0.5 mg/day treatment was started.
After four weeks of treatment abdominal distension and dyspnea were dissolved and laboratory tests were normalized. The patient was discharged at 14th weeks of gestation. She was seen at regular visits and delivered uneventfully at the 37th week of pregnancy.

**Discussion**

Ovarian hyperstimulation syndrome (OHSS) is an iatrogenic complication of exogenous gonadotropins or sometimes clomiphene citrate used for ovulation induction. The incidence is about 1-10% and the severe form constitutes about 1-2% of the cases. Major risk factors are: young age, PCOS, lean body weight, high dose gonadotropins use, elevated estradiol and human chorionic gonadotropin (hCG) levels, previous OHSS, molar pregnancy, multiple pregnancy and hypothyroidism. This case had none of these risk factors. Molecular FSH receptor gene defects have been shown in recurrent OHSS cases in some families. There was not such a finding in our case.

Spontaneous OHSS is a rare entity. De Leener et al. classified spontaneous OHSS into three types: Type I: caused by FSH receptor mutations; Type II: caused by elevated hCG; Type III: hypothyroidism related. In both type I and type II development of OHSS is hCG mediated. Mutations in FSH receptors may cause increased sensitivity to hCG. Although there is a case of spontaneous OHSS in a non-pregnant adolescent with recurrent OHSS almost all cases in the literature were pregnant. In this case, since our center does not have the necessary set up, we could not test for FSH receptor mutations.

Vascular endothelial growth factor (VEGF) is blamed as the cause of fluid loss to the third space, hypovolemia, hemoconcentration and electrolyte imbalance. VEGF changes the structure of endothelial gap junctions and increases vascular permeability. In this case we saw pleural effusion, ascites, hemoconcentration, hypovolemia, and vulvar edema assumed to be related to VEGF. Expression of VEGF mRNA has been shown to be induced by hCG in a dose- and time-dependent fashion. It was shown that VEGF mRNA expression is increased after luteinizing hormone (LH) surge. Molecular similarity between LH and hCG is important for both progression of the disease and prevention strategies. Dopamine receptor-2 agonist activation decreases ovarian VEGF production and prevents vascular permeability in OHSS rat models. Polymorphism of VEGF receptor gene itself may also be associated with the occurrence of OHSS.

OHSS can be classified as mild, moderate, and severe. Mild and moderate cases have a good prognosis, usually recovering spontaneously or with conservative management. Severe cases need inpatient care. This was a case of severe OHSS. In the management of these patients, close follow up of vitals, body weight, abdominal circumference, and fluid balance is crucial. Blood tests must be checked frequently. Hyponatremia is a common finding in these patients. Crystalloids are the first choice for fluid replacement. Daily fluid needs change from 1.5 to 3 L. Volume expanders such as dextran, albumin, hydroxyethyl starch (HES), and fresh plasma can also be
used. Prophylactic use of heparin is necessary for thromboprophylaxis in patients at risk of thromboembolism. Cabergoline is a dopamine receptor agonist that decreases vascular permeability by inhibiting VEGF receptors. Steroids are effective since there is an inflammatory response in OHSS. In our case cabergoline and steroids were used since there was a progression in the disease. After 4 weeks of treatment, clinical and laboratory findings were normalized in our case and the patient was discharged from the hospital. She delivered uneventfully at 37th week of gestation. Cabergoline, when given at the time of diagnosis of OHSS, appears to work rapidly and effectively to diminish the clinical symptoms of the disease.

Conclusion

Severe OHSS is a life threatening complication of ovarian hyperstimulation. Spontaneous OHSS is a rare entity, which occurs in gestations without ovulation induction. Early diagnosis may prevent unwanted results of the disease.

References


