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Case report

Ovarian hyperstimulation syndrome (OHSS) in spontaneous pregnancy

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ABSTRACT

It has been known that most cases of ovarian hyperstimulation syndrome (OHSS) are almost exclusively associated with controlled ovarian stimulation with gonadotrophins or occasionally, clomiphene citrate. However, OHSS is also infrequently associated with a ontaneous ovulatory cycle, usually in the case of multiple gestations, hypothyroidism, or severe forms of polycystic ovarian syndrome. Severe OHSS associated with a spontaneously conceived prhyperstimulation syndrome (sOHSS) in a woman who conceived spontaneously with no underlying disease. All associated risk factors were excluded, such as multiple gestations, hypothyroidism, or polycystic ovarian syndrome. Purpose of this case report is to discuss about the condition which can be associated morbidity and even mortality, if remain undiagnosed and if not managed properly. Furthermore, it is interesting to note that exploratory laparotomy was performed in six cases, because an ovarian cancer was suspected. Therefore, clinicians must bear the differential diagnosis of OHSS in mind if a patient presents with gross ascites and other symptoms of ovarian cancer, which also may be signs of OHSS. This case report emphasis that by taking all possible differential diagnoses

into account, unnecessary laparotomy may be avoided pregnancy is are with only few previous reports.

1. Introduction

The ovarian hyperstimulation syndrome (OHSS) has been extensively documented in literature as an iatrogenic complication (Ayhan A et al., 1996; Ludwig M et al., 1998). Mild and moderate forms of OHSS are common; affecting 8-23% and 1-7% of *vitro* fertilization (IVF) respectively, whereas severe OHSS is rare affecting 0.5% of IVF (Navot D et al., 1992). Less frequently OHSS can occur after mild ovarian stimulation using clomiphene citrate (Chow, 1984). Clinical manifestations can have a spectrum ranging from nausea, vomiting, abdominal discomfort and distensions to potentially life-threatening complications. The symptoms are more severe and persist longer if pregnancy is successful (Smits G, et al; 2003). Although the presence of human chorionic gonadotropin is invariably associated with the condition, the pathophysiological mechanism remains undefined; the underlying mechanism responsible for the clinical manifestations of OHSS appears to be neoangiogenesis and increased capillary permeability of enlarged ovarian and other endothelial surfaces (Smits G, et al, 2003).

Severe spontaneous ovarian hyperstimulation syndrome (sOHSS) associated with spontaneously conceived pregnancy is rare with only few previous reports, usually in case of multiple gestations, hypothyroidism, young age, severe forms of polycystic ovarian syndrome (PCOS)**,** hydatiform mole, triploidy or mutations of FSH (follicle-stimulating hormone) receptor (FSHR) gene.

We report, herein, a case of sOHSS in a woman who conceived spontaneously complicated by ascites and decreased urine output. All associated risk factors mentioned earlier were excluded, and there was no history of ovarian stimulation and HCG (human chorionic gonadotropin) use.

She was managed conservatively, in order to avoid unnecessary laparotomy, we emphasize the importance of careful diagnosis in order to differentiate sOHSS from ovarian cancer.

2. Material and methods (case report)

A 29-year-old woman Gravida 4, Para 3+0 was referred to our ICU (intensive care unit) with 10 weeks viable intrauterine pregnancy, vomiting, nausea, severe lower abdominal pain, abdominal distention and oligouria. On admission, her blood pressure was 110/60 mm Hg, heart rate 96 beat/minute and respiratory rate of 26/min. Physical examination revealed distended, tense and tender abdomen with massive ascites (abdominal girth 96cm), with positive fluid thrill but no abdominal viscera was palpable. Pelvic examination revealed edematous right libia majora with milky discharge. Chest examination revealed cripitations.

A baseline work-up at ICU admission showed an total leukocyte count (TLC) of 12.9 x 10^3 /µl with 77.6% neutrophils, hemoglobin 9.8g/dl, hematocrit 31.3%, serum creatinine 0.51 mg/dl and serum albumin 30 gm/dl. Hepatic and coagulation profile were normal. Chest radiograph showed bilateral pleural effusion without any cardiomegaly. Human chorionic gonadotrophins was (βhCG) 264,26800mU/ml, Thyroid function tests were also normal, carcino embryonic antigen (CEA) value was 0.84ng/ml, cancer antigen (CA) 125 value was found to be >1000 IU/ml. Ultrasound abdomen revealed grossly enlarged bilateral ovary showing presence of multiple enlarged follicles of size > 13 cm along with ascites. On detailed evaluation, her past history did not revealed any history of controlled ovarian stimulation, using FSH (follicle-stimulating hormone) and HCG (human chorionic gonadotropin. Provisional diagnosis was OHSS; the other differentials considered were choriocarcinoma and ovarian tumor. But her ascetic fluid cytology was normal. We did not check for molecular biology study of mutations of FSH receptor (FSHR) gene because patient had already three (03) normal pregnancies.

During her ICU stay monitoring included parameters like body weight, blood pressure, input and output along with laboratory parameters. The patient condition was stable and oxygen saturation was maintained. She was managed conservatively with a multidisciplinary approach and intensive care monitoring. ICU management included controlled intermittent oxygen therapy, albumin therapy, antibiotics, low molecular

weight heparin for deep vein thrombosis prophylaxis and other supportive therapy, she was placed in propped up position. Renal function was supported by fluid replacement. She never required diuretics or dialysis support during her ICU stay.

She required repeated abdominal paracentesis due to massive ascites. Fortunately, the patient did not require thoracocentesis as her symptoms gradually subsided. The general condition of the patient improved gradually and patient was discharged after ICU stay of 15 days, and both the size of the ovaries and the ascites gradually decreased during the pregnancy. At term, the patient delivered a healthy male infant weighing 2860 g. Her intrapartum and postnatal period was uneventful.

3. Discussion

OHSS is an iatrogenic, serious complication associated with *in vitro* fertilization (IVF), whereas sOHSS has been reported in rare cases during pregnancy. We are writing this report after taking informed consent from the patient. To the knowledge of authors, the presented case is one of few examples of spontaneous OHSS.

Although pathophysiology of this syndrome has not been completely elucidated, but HCG, vascular endothelial growth factor (VEGF) and the involvement of the renin–angiotensin believed to responsible in the pathogenesis of OHSS, due to release of an ovarian hormonal factor responsible for the chain of events causing increased capillary permeability of enlarged ovarian and other endothelial surfaces (Elchalal and Schember, 1997).

However, endogenous factors that may operate to result in sOHSS were initially described by Rothmensch and Scommegna in 1989 in hypothyroid woman, while Zalel *et al.* (1992) reported spontaneous case due to underlying PCOS with endogenous luteinizing hormone and HCG surge.

Nevertheless, case reported here had neither clinical nor laboratory evidence of thyroid disorder and absence of hyperandrogenic signs as well as three (3) previous spontaneous term deliveries exclude a diagnosis of thyroid disorder, PCOS and mutations of FSHR gene. OHSS association with mutations of FSHR gene has been reported by Smits G et al., 2003.

The incidence of OHSS in spontaneous pregnancies must be even higher than few cases reported in world literature. However, it is interesting that exploratory laparotomy was performed in six cases, because advanced ovarian cancer was suspected due to typical clinical presentation with ascites and pleural effusion (Ayhan et al., 1996; Lipitz et al., 1996). Therefore, to avoid unnecessary laparotomy, clinicians must bear differential diagnosis of OHSS in mind; if a patient presents with gross ascites and other symptoms of ovarian cancer, which also may be signs of OHSS.

In this case patient developed respiratory distress secondary to massive ascites and massive pleural effusion which usually occurs in the severe form of OHSS. Management of OHSS is mainly supportive since the syndrome is self-limiting and resolution parallels the fall in hCG levels. Medical management is mainly to maintain circulatory function and prevent organ dysfunction. The intravascular volume should be maintained to prevent hemoconcentration and allow sufficient urine output. Initial fluid of choice is crystalloids (Avecillas JF et al, 2004). Patients with hematocrit more than 45% or hypoalbuminemia less than 30 gm/dl or ascites, human albumin is the plasma expander of choice. Once sufficient volume expansion has been achieved and the hematocrit is less than 36% frusemide should be given to assist the renal function. Premature or overzealous use of diuretics may aggravate hypovolemia and hemoconcentration leading to renal dysfunction and thromboembolism. Intravascular volume expanders like fresh frozen plasma and dextran has no advantage over albumin (Budev MM et al, 2005). In the presence of thromboembolism, therapeutic anticoagulation is indicated. The use of dopamine agonist cabergoline has been found to reduce the effects of VEGF-mediated vascular permeability without compromising implantation and pregnancy rates. Together, these treatments will complement the ongoing progress with other procedures such as *in vitro* maturation and oocyte vitrification, and enable physicians to improve the prediction and prevention of OHSS (Garcia-Velasco JA, 2009).In patients with hydrothorax who are not symptomatic, conservative management is sufficient. If the patient has respiratory symptoms, thoracocentesis should be done as but it was not needed in our case. If adult respiratory distress syndrome (ARDS) develops, patient should be ventilated with lung protective ventilation strategy.

Our patient was managed conservatively; abdominal paracentesis was also done for massive ascites. Fortunately, the patient did not require thoracocentesis as her symptoms subsided. The general condition of the patient improved gradually, with good fetomaternal outcome.

4. Conclusion

OHSS in spontaneous pregnancy is an extremely rare event; without the usual risk factor. Though rare, in order to ensure timely diagnosis and to prevent its complications and unnecessary intervention it should be managed with multidisciplinary approach; gynecologist and chest physicians should be more aware of this syndrome.

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