Severe ovarian hyperstimulation syndrome leading to ICU admission

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ABSTRACT

Severe ovarian hyperstimulation is a rare complication of ovulation induction therapy. In this report, we are presenting a case of 33-year female, who required intensive care unit admission due to respiratory failure secondary to massive pleural effusion and ascites. With the positive history of *in vitro* fertilization, the patient was diagnosed to have severe ovarian hyperstimulation syndrome. Besides the medical treatment, abdominal paracentesis for the drainage of massive ascites and tube thoracostomy were performed, resulting in gradual improvement.

Key words: *Ovarian hyperstimulation syndrome, ascites, pleural effusion*

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INTRODUCTION

Ovarian stimulation contributes to the overall effectiveness of *in vitro* fertilization treatment. However, ovarian stimulation is also associated with health risks and adverse events in the form of ovarian hyperstimulation syndrome (OHSS). The symptoms of OHSS can have a spectrum ranging form nausea, vomiting and mild abdominal discomfort to severe disease with ascites, pleural effusion and renal failure. We present a rare report of severe OHSS.

CASE REPORT

A 33-year-old woman with secondary infertility was referred to our ICU, because of severe breathlessness, decreased urine output, nausea, lower abdominal pain and abdominal distention. On admission, her blood pressure was 140/100 mm Hg, heart rate 88/min and respiratory rate of 32/min. Physical examination revealed pedal edema along with massive ascites (intraabdominal pressure 16 mm Hg). Chest examination revealed bilateral dull notes on percussion along with diminished air entry on auscultation suggestive of bilateral pleural effusion.

A baseline work-up at ICU admission showed an elevated total leukocyte count (TLC) of 30 100 with 89% neutrophils, hemoglobin 12.2 gm/dl, hematocrit 44.4%, serum creatinine 1.2 mg/dl and serum albumin 2.2 gm/dl. Arterial blood gas (ABG) on room air showed PaO_2 82 mm Hg, pH 7.3, $PaCO_2$ 30.6 mm Hg, HCO_3 16.3 mmol/L, base deficit of 8.1 and O_2 saturation of 95%. Hepatic and coagulation profile were normal. Chest radiograph showed bilateral pleural effusion (right>left) without any cardiomegaly. Echocardiography revealed normal contractility with no evidence of pericardial effusion. Pregnancy test was negative. 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 revealed that she had underwent controlled ovarian stimulation, using FSH (follicle-stimulating hormone) and HCG (human chorionic gonadotropin) preceding *in vitro* fertilization 2 weeks back. Thus she was diagnosed as a case of severe OHSS. During her ICU stay monitoring included parameters like body weight, intra-abdominal pressure, central venous pressure, invasive blood pressure, input and output along with laboratory parameters.

ICU management included controlled oxygen therapy by venture mask, albumin therapy, antibiotics, low molecular weight heparin for deep vein thrombosis prophylaxis and other supportive therapy. Renal function was supported by using diuretics (furosemide infusion at rate of 5 mg/h). She never required dialysis support during her ICU stay. For pleural effusion, chest tube was inserted on right side along with ultrasound-guided pleural fluid aspiration on left side. Single time abdominal paracentesis was also done for massive ascites. The general condition of the patient improved gradually and patient was discharged after ICU stay of 8 days.

DISCUSSION

OHSS is an iatrogenic, serious complication associated with *in vitro* fertilization (IVF).[1] The syndrome is typically associated with exogenous gonadotropin, rarely with clomiphene citrate and gonadotrophin releasing hormone. Without human chorionic gonadotrophin (hCG), OHSS is extremely rare. Spontaneous occurrence of OHSS has been reported in rare cases during pregnancy.[2] We are writing this report after taking informed consent from the patient.

The symptoms are more severe and persist longer if pregnancy is successful. Mild and moderate forms of OHSS are common, affecting 8–23 and 1–7% of IVF, whereas severe OHSS is rare affecting ~0.5% of IVF.[3-4] Similarly our case is one of the rare presentations of OHSS.

Although the pathophysiology of this syndrome has not been completely elucidated, 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, fluid shift from the intravascular space to the extravascular space (abdomen, pleura, pericardium), hemoconcentration, decreased renal clearance, oliguria/anuria, hyperviscosity of blood, modification in coagulation risk factors and thromboembolic risks.[5] Vascular endothelial growth factor (VEGF) has a major role in the pathogenesis of OHSS. hCG either endogenous (pregnancy derived) or exogenous induces the release of VEGF.[6-7] VEGF is a heparin-binding glycoprotein with vascular permeability enhancing, angiogenic and endothelial cell-specific mitogenic activities.[8] VEGF levels correlates with severity of OHSS.[6-7] The process is self-limiting as the hCG effect decreases unless fetal hCG begins to be secreted.

Symptoms of OHSS usually begin with a sensation of bloating, abdominal discomfort, nausea, vomiting and diarrhea. As the disease progresses, accumulation of fluid in the third space leads to ascites, pleural and pericardial effusion, hypovolemia, oliguria, hemoconcentration and electrolyte imbalance.[9-11] In our case the disease progressed to the extent that she developed respiratory distress secondary to massive pleural effusion and massive ascites. Pleural effusion usually occurs in the severe form of OHSS.[12,13] In our case, bilateral effusion occurred during the initial days of treatment, which is rare.

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.[1,14] 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.[15] Intravascular volume expanders like fresh frozen plasma and dextran has no advantage over albumin.[15] In the presence of thromboembolism, therapeutic anticoagulation is indicated.[16] The use of dopamine agonist cabergoline has been found to reduce the effects of VEGF-mediated vascular permeability without compromising implantation and pregnancy rates.[17] 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.[17]

In patients with hydrothorax who are not symptomatic, conservative management is sufficient. If the patient has respiratory symptoms, thoracocentesis should be done as it was done in our case. If adult respiratory distress syndrome (ARDS) develops, patient should be ventilated with lung protective ventilation strategy. In severe OHSS, prophylactic anticoagulation should always be used because of hypercoagulable state.

In conclusion, severe OHSS should be considered in any women presenting with ascites and pleural effusion with history of controlled ovarian stimulation. Though rare, the intensivists should be aware of this syndrome and should be managed with multidisciplinary approach along with obstetricians help. If left untreated, OHSS can result in serious health complications and even death.

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