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.

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 from 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 PaO2 82 mm Hg, pH 7.3, PaCO2 30.6 mm Hg, HCO3 16.3 mmol/L, base deficit of 8.1 and O2 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.

Key words: Ovarian hyperstimulation syndrome, ascites, pleural effusion

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ICU management included controlled oxygen therapy by
ventilator 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
clonomophone 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.[9-15] 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 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.

**REFERENCES**

1. Whelan JG 3rd, Vlahos NF. The ovarian hyperstimulation
2. Smits G, Olatunbosun O, Delbaere A, Pierson R, Vassart G, Costagliola S. Ovarian hyperstimulation syndrome due to a mutation in the follicle-stimulating hormone receptor. N Engl J Med 2003;349:760-6.

3. Golan A, Ron-al R, Herman A, Soffer Y, Weinraub Z, Caspi E. Ovarian hyperstimulation syndrome: An update review. Obstet Gynecol Surv 1989;44:430-40.

4. Navot D, Bergh PA, Laufer N. Ovarian hyperstimulation syndrome in novel reproductive technologies: Prevention and treatment. Fertil Steril 1992;58:249-61.

5. Polishuk WZ, Schenker JG. Ovarian overstimulation syndrome. Fertil Steril 1969;20:443-50.

6. Geva E, Jaffe RB. Role of vascular endothelial growth factor in ovarian physiology and pathology. Fertil Steril 2000;74:429-38.

7. Levin ER, Rosen GF, Cassidenti DL, Yee B, Meldrum D, Wisot A, et al. Role of vascular endothelial cell growth factor in ovarian hyperstimulation syndrome. J Clin Invest 1998;102:1978-85.

8. Ferrara N, Houck KA, Jakeman LB, Winer J, Leung DW. The vascular endothelial growth factor family of polypeptides. J Cell Biochem 1991;47:211-8.

9. Schenker JG, Weinstein D. Ovarian hyperstimulation syndrome: A current survey. Fertil Steril 1978;30:255-68.

10. Shanbhag S, Bhattacharya S. Current management of ovarian hyperstimulation syndrome. Hosp Med 2002;63:528-32.

11. Balasch J, Fábregues F, Arroyo V, Jiménez W, Creus M, Vanrell JA. Treatment of severe ovarian hyperstimulation syndrome by a conservative medical approach. Acta Obstet Gynecol Scand 1996;75:662-7.

12. Man A, Schwarz Y, Greif J. Pleural effusion as a presenting symptom of ovarian hyperstimulation syndrome. Eur Respir J 1997;10:2425-6.

13. Loret de Mola JR, Arredondo-Soberon F, Randle CP, Tureck RT, Friedlander MA. Markedly elevated cytokines in pleural effusion during the ovarian hyperstimulation syndrome: Transudate or ascites? Fertil Steril 1997;67:780-2.

14. Aveillas JF, Falcone T, Arroliga AC. Ovarian hyperstimulation syndrome. Crit Care Clin 2004;20:679-95.

15. Budev MM, Arroliga AC, Falcone T. Ovarian hyperstimulation syndrome. Crit Care Med 2005;33:301-6.

16. Practice committee of the american society for reproductive medicine. Ovarian hyperstimulation syndrome. Fertil Steril 2004;82:581-6.

17. Garcia-Velasco JA. How to avoid ovarian hyperstimulation syndrome: A new indication for dopamine agonists. Reprod Biomed Online 2009;18:71-5.

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