Ovarian Hyperstimulation Syndrome (OHSS) in Pregnancy- Case Report

Hemant G Deshpande, Shankar B Burute, Karuna Ratwani, Chandrakant S Madkar, Sumit Jethani

Abstract— **INTRODUCTION**: Ovarian hyperstimulation syndrome caused by injection of human chorionic gonadotropin (hCG) presented with wide spectrum of clinical and laboratory signs and symptoms ,ovarian enlargement and fluid shift from intravascular space to third space.
CASE DESCRIPTION: A 25 yr female $G_2P_1L_0$ came with complaints of pain in abdomen ,burning micturition, abdominal distension, nausea and vomiting. She came with weak urine pregnancy test (UPT) positive .No other history of irregular menses, hirsutism or any other complaints.Ultrasound (USG) (24/4/13) s/o single intrauterine gestation sac with true decidual reaction large complex cyst in left ovary(13.8 X 6.0 X7.7cms) and large right ovarian cyst (9.8 X 7.5 X 6.7cms).On examination soft, left side lump formed around 7X7 cms, mobile mass, palpable mild tenderness present more on left side on per abdomen. On pv examination left sided adnexal mass around 7X7 cms ,mobile mass,not seperated from uterus,tenderness present ,right fornix lump palpable of 5X5 cms .Laboratory findings were unremarkable. Management consisted of plenty of fluids , abdominal girth monitoring & input output monitoring and analgesic for pain.
Index Terms— Ovarian hyperstimulation syndrome(OHSS), human chorionic gonadotropin (hCG), urine pregnancy test (UPT), Ultrasound (USG)

1 INTRODUCTION

Ovarian Hyper stimulation Syndrome (OHSS) is a syndrome with a wide spectrum of clinical and laboratory symptoms and signs , ovarian enlargement and a fluid shift from intravascular space to third space due to increased permeablity manifesting as ascites ,pleural effusion , hemoconcentration , oliguria, electrocyte imbalance and hypercoagulability .
Ovarian hyper stimulation syndrome is particularly associated with injection of a hormone called human chorionic gonadotropin(hCG) which is used for inducing final oocyte maturation and/or triggering oocyte release. The risk is further increased by multiple doses of hCG after ovulation and if the procedure results in pregnancy[1] Using a GnRH agonist instead of hCG for inducing final oocyte maturation and/or release results in an elimination of the risk of ovarian hyper stimulation syndrome, but a slight decrease of the delivery rate of approximately by 6% [2].

CASE REPORT:
A 25 year old female G2P1L0 with UPT positive (faint) presented with c/o pain in abdomen and distension ,pv mucoid discharge ,burning micturition,nausea & vomitting . Patient gives no history of hirsutism, weight gain, weight loss , irregular menses. No history of fever , cold,cough, diarrohea,breast discharge.
USG(24/4/13) s/o single intrauterine gestation sac with true decidual reaction large complex cyst in left ovary (13.8 X 6.0 X7.7cms) and large right ovarian cyst (9.8 X 7.5 X 6.7cms)
LMP 24th March 2013
EDD 31st Dec 2013 2-3 days/ 28-30 days/ RMF
Past menstrual history :
2-3 days/ 28-30 days/ RMF no dysmenorrhea or passage of clots
Obstetric History : Married life 10 years P1D1 – Male child/6 yrs/ still birth Patient had taken infertility treatment for 3 years .
Past History :
No history of TB/DM/ HTN/ Asthma/ Epilepsy/Jaundice, No history of major medical or surgical illness .On examination general condition fair, averagely built and nourished, afebrile, Pulse- 78 beats per minute regular on both sides , normal in rhythm , volume, BP- 110/70 mm of Hg in supine position on both sides,Cardio vascular system/ Respiratory System-No Abnormal Deformity.
On per abdomen Soft, left side lump formed around 7X7 cms mobile mass, palpable .Mild tenderness present more on left side
On per speculum cervix and vagina healthy
On per vaginum left sided adnexal mass around 7X7 cms .Mobile mass, not seperated from uterus.Tenderness present. Right fornix lump palpable of 5X5 cms.

Figure 1. Cyst seen In USG Report

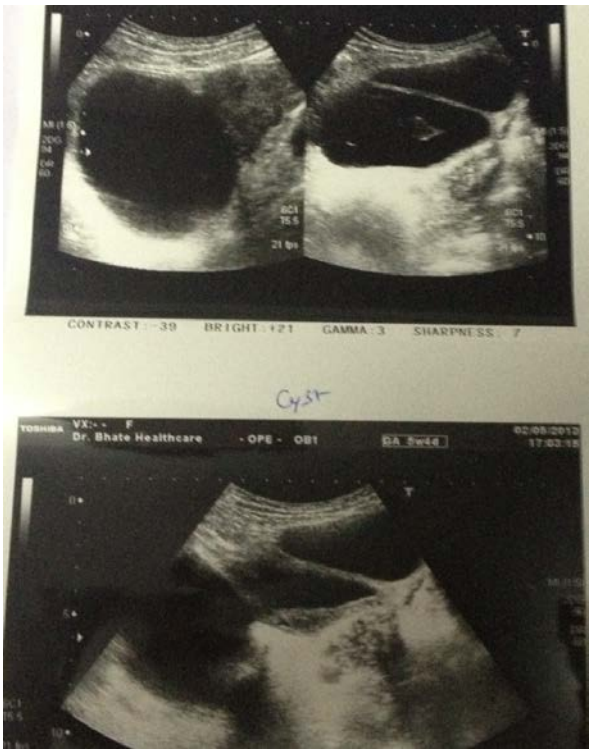


Figure 2. Shows Necklase sign seen in Ovary

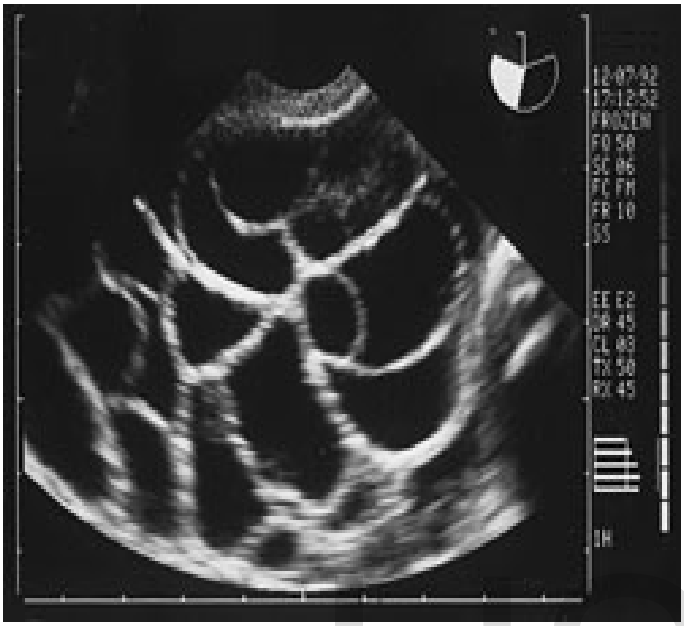
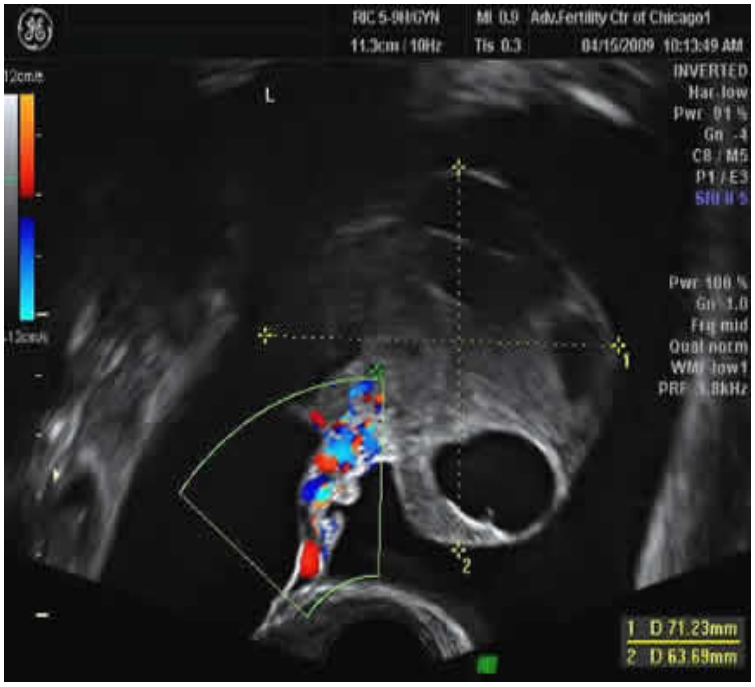


Figure 3. Shows Hyperstimualted Ovary



DISCUSSION:

Incidence of Mild form is 8-23%, Moderate form is 0.005-7% and Severe form is 0.005-2%.It presents after hCG administrations or rise of hCG due to an early pregnancy . It can be early onset within 3-7 days of hCG administration or late onset 12 to 17 days after ovulation because of early pregnancy. It is usually seen in young females less than 35 years of age,in females having polycystic ovarian disease with necklace sign present of ovary and more than 35 follicles present in ovary on sonography.

CLASSIFICATION – NAVOTS

MILD :Ovaries are enlarged (5-12 cms) with ascites with mild abdominal distension. Abdominal pain, Nausea, diarrhea [3]

SEVERE :Ovaries enlargement(>12 cms). Ascites, Hemoconcentration ,thrombosis, abdominal distension, oliguria, pleural effusion , respiratory disease Hematocrit>45% ,WBC> 15000 ,S.Creatinine 1-1.5g/dl ,Creatinine clearance>50% ,Anasarca.Liver enzymes elevated.

CRITICAL: Enlarged ovary , tense ascites with hydrothorax & pericardial effusion Heamatocrit >55%, WBC>25000, oligoanuria, S.creatinine>1.6g/dl , renal failure, thromboembolic phenomena , ARDS

The complicated pathophysiology has still not been completely elucidated .

Two major events are

Neovascularization

Increased vascular permeablity of mesothelial surface

The increased capillary permeablity of the ovarian vessels and the other mesothelial surfaces lead to acute fluid shift to third space .This is triggered by release of vasoactive substances secreted by ovary under influence of Hcg.

Interleukins & OHSS: Interleukin 1 may cause capillary permeablity , hemoconcentration and other acute phases responses. Interleukin 6 is seen in follicular fluid & plasma of patients of OHSS. It increases the capillary permeablity & neovascuarization.

Nitric oxide in OHSS :It causes increase in vascular permeablity & leakage of fluid from blood vessels into extravascular space. Vasoactive substances like angiotensin converting enzyme ,histamine,bradykinin & thrombin are known to stimulate nitric oxide synthesis .

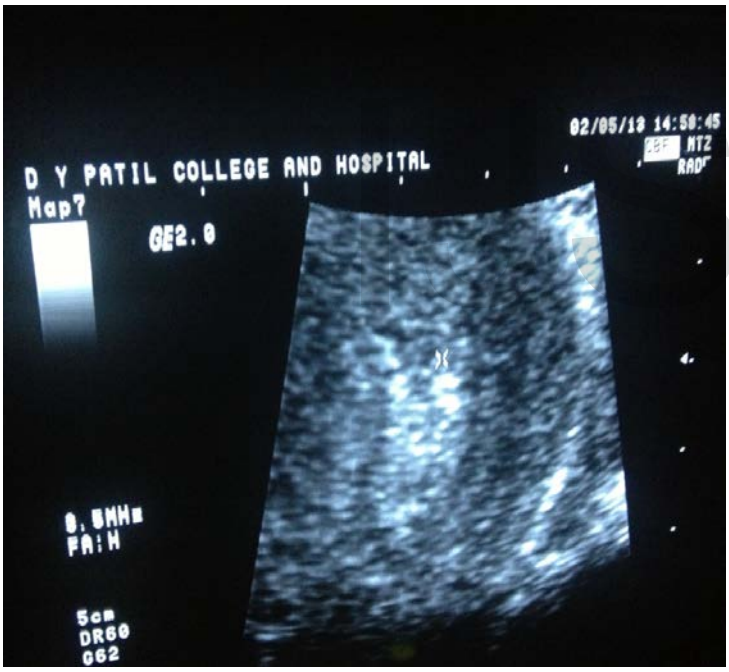
Vascular endothelial growth factor(VEGF): It is a vasoactive glycoprotein ,originating from the enlarged ovary , with a high specificity for endothelial cells & induces proliferation & angiogenesis. It provokes extravascular fluid accumulation and elevated plasma concentration of vWF which is known to cause OHSS.

Patient comes with complains of

lower abdominal pain & distension ,

GI disturbances like nausea ,vomitting & diarrohea ,
progressive lethargy,
history of decreased urine output,
increased pulse ,shortness of breath ,fluid collection at base of lungs ,
significant fluid electrolyte imbalance,
Dehydration in severe case,
Hypercoagulability of blood causing thrombosis
Patient can give similar complaints in acute appendicitis, cholecystitis, ovarian cysts, 0varian torsion, pelvic inflammatory disease/ tuboovarian mass, pericardial effusion, peritonitis , abdominal sepsis, pleural effusion and pulmonary embolism .
Patient comes with complications of Ovarian torsion,Ovarian rupture,Thrombophlebitis,Renal Insufficiency.
Symptoms generally resolve in 1-2 weeks but will be more and persist longer if pregnancy occurs. This is due to HCG acting on corpus luteum in the ovaries sustaining the pregnancy before placenta develops Typically in severe OHSS with developing pregnancy the duration does not exceed first trimester .[3]

Figure 4. Shows decidual reaction



PREVENTION: Risk of OHSS is reduced by monitoring of FSH therapy to use this medication judiciously, and by withholding hCG medication.
Cabergoline confers a significant reduction in the risk of OHSS in high risk women according to a Cochrane review of randomized studies, but the included trials did not report the live birth rates or multiple pegnancy rates [4]. Cabergoline, as well as other dopamine agonists, might reduce the severity of OHSS by interfering with the VEGF system[5]. A systematic review and meta-analysis concluded that prophylactic treatment with cabergoline reduces the incidence, but not the severity of OHSS, without compromising pregnancy outcomes[6].
The risk of OHSS is smaller when using GnRH antagonist protocol instead of GnRH agonist protocol for suppression of ovulation during ovarian hyperstimulation.[7]The underlying mechanism is that, with the GnRH antagonist protocol, initial follicular recruitment and selection is undertaken by endogenous endocrine factors prior to starting the exogenous hyperstimulation, resulting in a smaller number of growing follicles when compared with the standard long GnRH agonist protocol[7].
Administration of human albumin or hydroxyethyl starch confers a significant decrease in severe OHSS, with no statistically significant evidence of decreased pregnancy rate.[4] Routine oocyte cryopreservation does not have evidence of preventing OHSS.[4] Also, coasting, which is ovarian hyperstimulation without induction of final maturation, does not significantly decrease the risk of OHSS[4].
MANAGEMENT:
INVESTIGATIONS
General condition : regular charting of vital signs – respiratory rate,pulse rate, temperature, weight charts ,abdominal girth measurement, strict input output chart
Biochemical tests – hematocrit,electrolytes, liver function tests,kidney function tests , coagulation profile, blood gases & acid base balance , serum hCG .
Ultrasonography[8] –ovarian size,amount of ascites, presence of hydrothorax,pregnancy

TREATMENT
The condition usually resolved within 0-14 days . Treatment is based on severity of disease.
MILD : Treatment is usually conservative and is done outpatient level with close follow up by reassuring the patient,plenty of fluids, avoiding exertion, counsel on warning signs,biochemical tests should be done along with USG,analgesics if required,and intake output monitoring .
Indications of hospitalization: Intolerable nausea & vomitting, hypotension, signs of pleural effusion,ascites, hematocrit>48% , Sodium <135 mg/l, Pottasium >5 mg/L, S.creatinine >1.2mg.
Maintenance of intravascular volume Normal saline with or without glucose is main crystalloid used for replacement. Upto 1.5-3 litres may be needed. Due to loss of proteins in third space plasma expanders may be used Low salt albumin is

expander of choice. It is given in a dose of 50-100 gms every 2-12 hrs

Prevention of thrombosis: Low dose heparin should be given where there is altered coagulation profile as a prophylaxis.

Management of ascites by paracentesis, where there is discomfort, compromise of venous return leading to decreased cardiac output & hypotension, renal compromise, respiratory distress. Under USG guidance upto 4 L of fluid can be withdrawn transabdominally or transvaginally.

Laprotomy : Laprotomy is required if cysts undergo torsion or hemorrage or rupture

CRITICAL OHSS

Renal failure: Dopamine may be required to dilate renal vasculature & improve blood flow. Central venous pressure line is put to monitor fluid. Hemodialysis may be required in severe cases.

Pulmonary compromise: Patients who do not respond to paracentesis , diuresis may need ABG monitoring, thoracocentesis or assisted ventilation.

Thromboembolic events : Therapeutic anticoagulation of heparin

Termination of pregnancy :If critical condition does not improve termination of pregnancy should be done.

CONCLUSION:

OHSS is a preventable condition & implementation of evidence based prevention strategies should enable to significantly reduce its occurrence .Improved understanding of its pathogenesis and more accurate IVF protocols helps in minimizing OHSS. GnRH agonists appear to be new therapeutic strategy to reduce OHSS.

Refrences

[1] Ovarian hyperstimulation syndrome Updated by: Linda J. Vorvick and Susan Storck Update. Also reviewed by David Zieve. Date: 7/27/2009

[2] Humaidan, P.; Kol, S.; Papanikolaou, E.; Copenhagen GnRH Agonist Triggering Workshop Group (2011). "GnRH agonist for triggering of final oocyte maturation: time for a change of practice?". Hum. Reprod. Update 17 (4): 510–524.

[3] Textbook of Assisted Reproductive Techniques, Laboratory and Clinical Perspectives, edited by David K. Gardner, 2001

[4] Farquhar, C.; Rishworth, J. R.; Brown, J.; Nelen, W. L. M.; Marjoribanks, J. (2013). "Assisted reproductive technology: an overview of Cochrane Reviews". In Brown, Julie. Cochrane Database of Systematic Reviews.

[5] Gomez, Raul (2006). "Low-Dose Dopamine Agonist Administration Blocks Vascular Endothelial Growth Factor (VEGF)-Mediated Vascular Hyperpermeability without Altering VEGF Receptor 2-Dependent Luteal Angiogenesis in a Rat Ovarian Hyperstimulation Model". Endocrinology 147 (11): 5400–5411.

[6] Youssef MA, van Wely M, Hassan MA, et al. (March 2010). "Can dopamine agonists reduce the incidence and severity of OHSS in IVF/ICSI treatment cycles? A systematic review and meta-analysis". Hum Reprod Update 16 (5): 459–66.

[7] La Marca, A.; Sunkara, S. K. (2013). "Individualization of controlled ovarian stimulation in IVF using ovarian reserve markers: From theory to practice". Human Reproduction Update 20: 124..

[8] Horwitz, et al. Ovarian Hyperstimulation Syndrome: Treatment and Medication. eMedicine obstetrics and gynaecology 11/2008. http://emedicine.medscape.com/article/1343572-treatmen

.

Dr Hemant G Deshpande is Currently Professor and Head in Department of Obstetrics and Gynaecology at Dr DY Patil Medical College. Pune.
Mob No: +919422033660
Dr Shankar BBurute is Professor in Department of Obstetrics and Gynaecology at Dr DY Patil Medical College ,Pune
Dr Karuna Ratwani is currently pursuingMaster of Surgery course in Obstetrics and Gynaecology at Dr DY Patil Medical College, Pune
Dr Chnadrakant S Madkar is Professor in Department of Obstetrics and Gynaecology at Dr DY Patil Medical College. Pune
Dr Sumit Jethani, Assistant Professor in Department of Community Medicine at Dr DY Patil Medical College,Pune