

Case Report

Severe Spontaneous Ovarian Hyperstimulation Syndrome With Cervical Insufficiency: A Case Report

Emine Demirel^{1*}, Ugur Turhan¹, Emre Ekmekci¹, Aslı Subasioglu² and Sefa Kelekci¹

¹Department of Obstetrics and Gynecology, Faculty of Medicine, Izmir Katip Celebi University, Izmir, Turkey

²Division of Medical Genetics, Atatürk Training and Research Hospital, Izmir Katip Celebi University, Izmir, Turkey

Abstract

Objective: Spontaneous OHSS (sOHSS) is an extremely rare condition in natural conceived pregnancy, it's most often seen in cases of multiple or molar gestations, hypothyroidism and polycystic ovary syndrome. Severe form is a rare entity in singleton pregnancy with spontaneous ovulation and may cause laparotomy because of misdiagnosis such as ovarian tumors or severe complications. We report a rare case of spontaneous severe OHSS.

Case report: We report a rare case of spontaneous severe OHSS accompanied by cervical insufficiency at second trimester in singleton pregnancy. The patient was applied at 11th weeks of gestation with abdominal pain, dyspnea, ascites that was diagnosed OHSS. We managed expectantly without complications.

Conclusion: Although spontaneous OHSS a rare condition, it's important to consider OHSS in cases of bilateral enlarged cystic ovaries in pregnancy. Early diagnosis and successful management is essential to avoid serious complications, which may develop rapidly and may lead significant morbidity and mortality.

Keywords: Ascites; Pregnancy; Spontaneous ovarian hyper stimulation syndrome

Introduction

Ovarian hyper stimulation syndrome (OHSS) is a potentially life-threatening pharmacological complication of supraphysiological ovarian stimulation and incidence is increasing world-wide through the expansion of controlled ovarian hyper stimulation (COH) cycles. Severe OHSS complicates 1% of IVF cycles and is characterized by tremendous ovarian sizes (greater than 10 cm diameter) associated with abdominal distension, ascities, pleural effusion and hypovolemia [1]. Although thromboembolic phenomena, acute hepato-renal failure, acute respiratory distress syndrome and death were reported in severe cases, the true mortality rate of OHSS is unknown [2].

Severe OHSS is very rare in spontaneous ovulation cycles and always reported during pregnancy. Spontaneous OHSS (sOHSS) tends to present in late first trimester after 8-14 weeks of gestation, although iatrogenic OHSS usually occurs earlier [1]. High hCG levels (as in molar or multiple gestations), high TSH levels, FSH receptor (FSHr) mutations are accused for sOHSS and sOHSS is associated with pituitary tumors, familial predisposition, polycystic ovary syndrome, factor V Leiden mutation [3,4]. Here we reported a severe sOHSS case during singleton pregnancy.

Case Presentation

A 21-year-old primigravid patient is applied to our clinic at 11 weeks gestation due to severe abdominal pain, progressive abdominal swelling, pelvic pain and dyspnea. Her medical and family history was unremarkable. She did not have any medication for ovulation induction and her pregnancy was a spontaneous cycle. Her menstrual periods were regular.

She was severe dyspneic and bilateral pleural effusion was detected on chest x-ray. The vital signs were normal. The bowel sounds were normoactive. Transabdominal ultrasound scan revealed a singleton, intrauterine 11 weeks pregnancy with bilateral enlarged multicystic ovaries and a large amount of ascites fluid in pelvis and abdominal cavity (Figure 1) consistent with severe sOHSS. Right ovary was 18 cm

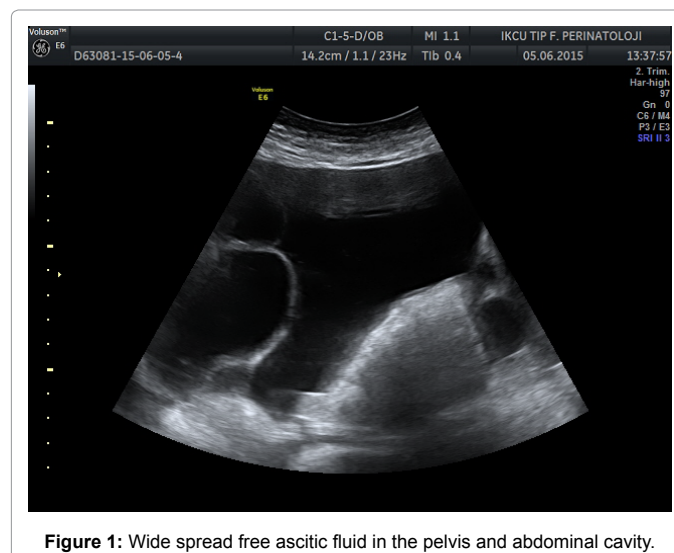


Figure 1: Wide spread free ascitic fluid in the pelvis and abdominal cavity.

and left one was 17 cm in diameter (Figure 2). Swiss-cheese appearance is detected in placenta sonographically. Liver and kidney were normal in sonography.

Preliminary blood tests revealed a hematocrit (Htc) of 36.2%, hemoglobin (Hb) of 11.2 g/dl, white blood cell count (WBC) of 10.660/mm³, platelet of 332.000/mm³, sodium of 128 mmol/l, potassium of 4.5

***Corresponding author:** Emine Demirel, Department of Obstetrics and Gynecology, Faculty of Medicine, Izmir Katip Celebi University, 170 Street, 35150 Karabaglar/Izmir, Turkey, Tel: +90 (232) 243 43 43; Fax: +90 (232) 243 15 30; E-mail: er_em.dr@hotmail.com

Received May 01, 2016; Accepted May 12, 2016; Published May 19, 2016

Citation: Demirel E, Turhan U, Ekmekci E, Subasioglu A, Kelekci S (2016) Severe Spontaneous Ovarian Hyperstimulation Syndrome With Cervical Insufficiency: A Case Report. JFIV Reprod Med Genet 4: 181. doi:10.4172/2375-4508.1000181

Copyright: © 2016 Demirel E, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

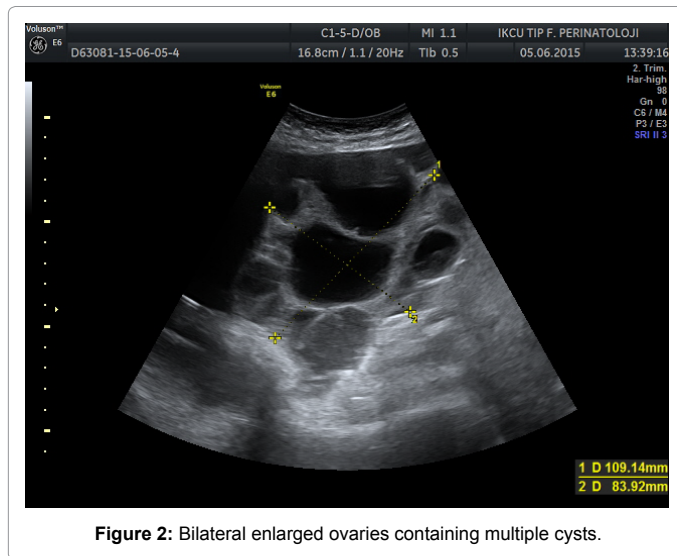


Figure 2: Bilateral enlarged ovaries containing multiple cysts.

mmol/l, calcium of 8 mg/dl, serum proteins of 4.9 g/dl with albumin of 2.6 g/dL, serum hcg of 630.631 mU/ml, total testosterone of 258 ng/dl, with other blood results including TSH, blood coagulation, renal function, liver function, free testosterone, prolactin and serologic tests within normal limits. There was no available testing for FSH receptor (FSHR) mutation in our hospital. There wasn't any significant pathological finding on pituitary MRI.

We obtained molecular genetic analysis for evaluation of Factor V Leiden mutation, prothrombin gene (20210G>A) mutation, methyltetrahydrofolate reductase (MTHFR) gene polymorphisms (MTHFR 677C>T and MTHFR 1298A>C), β -fibrinogen Hae III (-455 G>A) gene mutation, factor XIII Val34Leu (100 G>T) gene mutation, PAI-1 4G/5G gene mutation. Her results demonstrated that she was homozygous for PAI-1 4G/5G gene and heterozygous for MTHFR 677C>T and MTHFR 1298A>C gene polymorphisms.

The patient is hospitalized due to severe sOHSS and managed with intravenous fluid replacement, albumin infusion, hydroxyethyl starch (HES), low molecular weight heparin for thromboprophylaxis and carefully monitored about the course of her symptoms, body weight, abdominal circumference.

After three days of hospitalization, her dyspnea and abdominal distension advanced due to progressive ascites. Abdominoperitoneal pig-tail perennal catheter is replaced and peritoneal fluid was drained by catheter about 1000-2000 ml/day to reduce the patients' discomfort. Free abdominal fluid cytology was benign. Because bilateral ovaries were still enlarging cabergoline 0.5 mg/day treatment was started. After 3 weeks from catheterization, abdominal ascites decreased and catheter was removed. Ultrasonography revealed that the both ovaries were 8 cm in diameter.

Combined screening test result was 1/276 risk and f β hCG was 3.93 MoM. At 16 weeks, amniocentesis and chorionic villous sampling were performed at the same time due to placental appearance and possible terms of molar gestation or a chromosomal abnormality. Karyotype was normal and placental histopathology was focal fibrin deposition at a small perivillous area.

At 17⁺⁶ week of pregnancy, 7 weeks after admission, her complaints were dissolved and the laboratory findings remained stable; she was discharged. Ultrasonography revealed that normal size of ovaries without ascites. Her weekly β hCG counts until 18 weeks, showed

rapidly declining trend like 630.631, 158.824, 132.466, 96.303, 81.905, 53.852mU/mL, respectively.

At 22⁺³ week of pregnancy, she underwent cerclage due to cervical failure with Y formation that was determined on outpatient department. The pregnancy progressed to term and a healthy female baby of 3400 g was delivered at 40 weeks of gestation. Postoperative placental histopathology was normal. Four weeks after delivery, on sonographic examination, both ovaries were normal in size and β hCG was negative. She was managed expectantly with no complications.

Discussion

OHSS is a systematic disease resulting from vasoactive products released by hyper stimulated ovaries and is considered to be a complication of treatment with ovulation inducing agents. However, OHSS may rarely be associated with spontaneous cycle pregnancy like this case.

Although the etiology still seems to be unclear, human chorionic gonadotrophin (HCG) administration is believed to initiate the release of an ovarian hormonal factor responsible for the chain of events causing increased capillary permeability on the peritoneal and pleural surfaces. There are reported few cases of sOHSS with hypothyroidism, PCOS or molar pregnancy. The recent identifications of mutations in the FSH receptor (FSHR) gene, which display an increased sensitivity to hcg, are accused about the development of sOHSS [5]. There are different mutations and polymorphisms identified in FSHR gene that can activate ovaries and cause OHSS or inactivate that can lead to sterility. In addition to the genes and receptors for FSH the genetic researches have indicated luteinizing/human chorionic gonadotrophin hormones [5-7]. Some recent researches remark anti-Müllerian hormone (AMH) signaling pathway in the pathogenesis of OHSS as it was mentioned that AMH may has an important regulatory effects on folliculogenesis [8-10]. As it is known that; leakage of intravascular fluids that cause ascites and haemoconcentration seen in OHSS, besides the genes mentioned above vascular endothelial growth factor (VEGF) can be a target while searching the underlying factor of OHSS [7]. Also, placental mesenchymal dysplasia associated with sOHSS which is the most likely pathogenesis of ovarian stimulation from placental mesenchymal dysplasia derived vascular endothelial growth factor [6].

In our study, we obtained molecular genetic analysis for thrombophilia. It is known that women with OHSS are at higher risk for thromboembolism because they are haemoconcentrated and usually immobile [11]. This is also one of the most dangerous complications of OHSS. There are only few reports that examined the prevalence of thrombophilia markers in women with OHSS [12,13]. Different changes in haemostatic markers found to be related with hypercoagulability, but up to date there is no single test is available for predict the condition [14]. Our case's results demonstrated that she was homozygous for PAI-1 4G/5G gene.

Plasminogen activator inhibitor-1 (PAI 1) also known as endothelial plasminogen activator inhibitor or serpin E1 is produced by endothelial, smooth muscle, liver cells and platelets and elevated PAI-1 is a risk factor for thrombosis and atherosclerosis [15].

PAI-1 plasma level increases during pregnancy and reaches at term, three times more than in the non-pregnancy levels. There is also another PAI existing that is called plasminogen activator inhibitor-2 (PAI-2) that is secreted only during pregnancy by the placenta. So associated with the high PAI levels hypofibrinolysis is commonly found in pregnancies with high thrombotic risk [16].

In addition she demonstrated that she was heterozygous for MTHFR 677C>T and MTHFR 1298A>C gene polymorphisms a genotype where hyperhomocystinemia is common [13].

The importance of these polymorphisms is related with hyperhomocystinemia. The studies on the MTHFR knockout mice showed earlier pathologic changes in their large vessel walls [17].

Although we detect some polymorphisms that related with thromboembolism, we didn't determine any complication at our patient. This can be a result of early clinical management with low molecular weight heparin. So; like previous studies we also suggest that molecular genetic analysis for thrombophilia markers with other serum thrombophilia screens may be considered for patients with OHSS syndrome [13,14,16,18]. Besides this; our case confirmed that effective treatment strategy that includes cabergoline which is dopamine agonist and has a role of antagonizing and blocking VEGF may potentially reduce the severity of OHSS and related complications [19].

Conclusion

Although spontaneous OHSS a rare condition, it is important to consider OHSS in cases of bilateral enlarged cystic ovaries in pregnancy. In spontaneous pregnancies, bilateral ovaries should be established in early pregnancy and in case of bilateral hyperstimulated ovaries, patient should be followed about OHSS. Early diagnosis, meticulous and successful management is essential for to obviate unnecessary interventions and to avoid serious complications, which may develop rapidly and may lead to significant morbidity and mortality if left untreated.

References

1. Patil HN, Roy R, Pal R, Roychowdhury J (2015) Spontaneous Late Onset OHSS in Singleton Pregnancy in 2nd Trimester: A Rare Case. *J Obstet Gynaecol India* 65: 50-53.
2. Panagiotopoulou N, Byersb H, Newmanb WG, Bhatiaa K (2013) Spontaneous ovarian hyperstimulation syndrome: case report, pathophysiological classification and diagnostic algorithm. *Eur J Obstet Gynecol Reprod Biol* 169: 143-148.
3. Leener AD, Montanelli L, Van Durme J, Chae H, Smits G, et al. (2006) Presence and absence of follicle-stimulating hormone receptor mutations provide some insights into spontaneous ovarian hyperstimulation syndrome pathophysiology. *J Clin Endocrinol Metab* 91: 555-562.
4. Murata Y, Ando H, Nagasaka T, Takahashi I, Saito K, et al. (2003) Successful pregnancy after bromocriptine therapy in an anovulatory woman complicated

with ovarian hyperstimulation caused by follicle-stimulating hormone-producing plurihormonal pituitary microadenoma. *J Clin Endocrinol Metab* 88: 1988-1993.

5. Smits G, Olatunbosun O, Delbaere A, Pierson R, Vassart G, et al. (2003) Ovarian hyperstimulation syndrome due to a mutation in the follicle-stimulating hormone receptor. *N Engl J Med* 349: 760-766.
6. Davoudian P (2015) Placental mesenchymal dysplasia associated with spontaneous ovarian hyperstimulation syndrome. *BMJ Case Rep*.
7. Rizk B (2009) Symposium: Update on prediction and management of OHSS. *Genetics of ovarian hyperstimulation syndrome. Reprod Biomed Online* 19: 14-27.
8. Peluso C, Fonseca FL, Gastaldo GG, Christofolini DM, Cordts EB, et al. (2015) AMH and AMHR2 polymorphisms and AMH serum level can predict assisted reproduction outcomes: a cross-sectional study. *Cell Physiol Biochem* 35: 1401-1412.
9. Wang L, Li H, Ai J, Yue J, Li Z, et al. (2015) Attenuated AMH signaling pathway plays an important role in the pathogenesis of ovarian hyperstimulation syndrome. *Am J Transl Res* 7: 1925-1938.
10. Wang L, Li H, Ai J, Zhang H, Zhao Y (2015) Possible involvement of single nucleotide polymorphisms in anti-Müllerian hormone signaling pathway in the pathogenesis of early OHSS in Han Chinese women. *Int J Clin Exp Pathol* 8: 9552-9559.
11. Murdoch AP, Evbuomwan I (1999) Severe complications of ovarian hyperstimulation syndrome are preventable. *Hum Reprod* 14: 2922-2923.
12. Levy G, Lucidi RS (2011) Thrombophilia and ovarian hyperstimulation syndrome: a case report. *Hawaii Med J* 70: 97-98.
13. Dulitzky M, Cohen SB, Inbal A, Seidman DS, Soriano D, et al. (2002) Increased prevalence of thrombophilia among women with severe ovarian hyperstimulation syndrome. *Fertil Steril* 77: 463-467.
14. Cesari M, Pahor M, Incalzi RA (2010) Plasminogen activator inhibitor-1 (PAI-1): a key factor linking fibrinolysis and age related subclinical and clinical conditions. *Cardiovasc Ther* 28: 72-91.
15. Mimuro J (1991) [Type 1 plasminogen activator inhibitor: its role in biological reactions]. *Rinsho Ketsueki* 32: 487-489.
16. Kasum M, Danolić D, Orešković S, Ježek D, Beketić-Orešković L, et al. (2014) Thrombosis following ovarian hyperstimulation syndrome. *Gynecol Endocrinol* 30: 764-768.
17. Ferrara F, Meli F, Amato C, Cospite V, Raimondi F, et al. (2005) A case of ovarian hyperstimulation syndrome associated with the methylenetetrahydrofolate reductase mutation gene. *Fertil Steril* 84: 218.
18. Levy G, Lucidi RS (2011) Thrombophilia and ovarian hyperstimulation syndrome: a case report. *Hawaii Med J* 70: 97-98.
19. Naredi N, Talwar P, Sandeep K (2014) VEGF antagonist for the prevention of ovarian hyperstimulation syndrome: Current status. *Med J Armed Forces India* 70: 58-63.

Citation: Demirel E, Turhan U, Ekmekci E, Subasioglu A, Kelekci S (2016) Severe Spontaneous Ovarian Hyperstimulation Syndrome With Cervical Insufficiency: A Case Report. *JFIV Reprod Med Genet* 4: 181. doi:[10.4172/2375-4508.1000181](https://doi.org/10.4172/2375-4508.1000181)

OMICS International: Publication Benefits & Features

Unique features:

- Increased global visibility of articles through worldwide distribution and indexing
- Showcasing recent research output in a timely and updated manner
- Special issues on the current trends of scientific research

Special features:

- 700+ Open Access Journals
- 50,000+ editorial team
- Rapid review process
- Quality and quick editorial, review and publication processing
- Indexing at major indexing services
- Sharing Option: Social Networking Enabled
- Authors, Reviewers and Editors rewarded with online Scientific Credits
- Better discount for your subsequent articles

Submit your manuscript at: <http://www.omicsgroup.org/journals/submission>