

Case report on spontaneous ovarian hyperstimulation syndrome following natural conception associated with primary hypothyroidism

**Smisha Sridev,
Sridev Barathan**

Department of Reproductive
Medicine, Parvathi Nursing
Home, KK Nagar, Chennai,
Tamil Nadu, India

Address for correspondence:

Dr. Smisha Sridev,
New No 24, Old No 798,
Jeevanandam Road,
KK Nagar, Chennai - 78,
Tamil Nadu, India.
E-mail: smishamp@gmail.com

Received: 15.11.2012
Review completed: 07.02.2013
Accepted: 13.04.2013

ABSTRACT

Spontaneous OHSS is a rare event in pregnancy following natural conception and only a few cases have been reported in the literature so far. This report is a case of spontaneously conceived pregnancy with Spontaneous OHSS and Primary hypothyroidism

KEY WORDS: Hypothyroidism, spontaneous ovarian hyper stimulation syndrome, thyroid stimulating hormone

INTRODUCTION

Spontaneous ovarian hyperstimulation (spontaneous OHSS) is extremely rare in naturally conceived pregnancies. OHSS in the absence of exogenous gonadotropins is very rare, and only a few cases have been reported in the literature.^[1-8] Van Wyk and Grumbach first described the combination of multicystic ovaries, juvenile hypothyroidism and precocious puberty in 1960, since then sporadic cases of this syndrome have been reported in pre-pubertal or adolescent girls.^[9-12] Few cases only have been reported for adults both gestational and non-gestational.^[1-8] Spontaneous OHSS likely to occur at 8-14 weeks of gestation, while iatrogenic OHSS usually occurs earlier at 3-8 weeks of gestation.^[13,14] The etiopathogenesis of spontaneous OHSS is not studied well.

CASE REPORT

A 22 year old primigravida with spontaneous conception, regular menstrual cycles, married for 3 months and no relevant past medical illness, no clinical or subclinical evidence of hypothyroidism in the past; attended the Department of Obstetrics at 7 weeks of gestation. She was asymptomatic, and ultrasound scan also revealed single live intrauterine pregnancy at 7 weeks and normal appearing ovaries. At 9 weeks of gestation, she developed vomiting,

diarrhoea and lower abdominal discomfort. Abdominal examination revealed a non-tender, mobile mass of approximately 10 cm × 10 cm in the right iliac fossa with no clinical evidence of ascites.

Ultrasound scan performed at 9 weeks of gestation revealed a single live intrauterine gestation corresponding to 9 weeks of gestation, bilaterally enlarged multicystic ovaries with right ovary measuring 10 cm × 8 cm, left ovary 8 cm × 6 cm and no ultrasonological evidence of ascites, pleural or pericardial effusion [Figures 1 and 2].

Started with levothyroxin 150 µg daily. The abdominal discomfort reduced from 14th week onward and the size of the ovaries normalized at 20 weeks. At 17 weeks of gestation, triple screening was performed, and the report showed low risk (1/6500) for chromosomal aneuploidies. Anomaly scan done at 20 weeks showed no fetal or placental anomalies and bilateral maternal ovaries were normal sized.

The patient delivered a term female baby weighing 3300 g at 39 weeks of gestation.

DISCUSSION

Spontaneous OHSS can occur both in pregnant and non-pregnant women. De Leener^[15] classified spontaneous OHSS syndrome into three types based on clinical

Access this article online

Quick Response Code:



Website:

www.jhrsonline.org

DOI:

10.4103/0974-1208.117164

presentation and FSH receptor mutation. Type I is associated with the mutated FSH receptor and this type may cause recurrent spontaneous OHSS. Type II is secondary to high levels of human chorionic gonadotropin (hCG) as in hydatiform mole and multiple gestation and is the most frequent one. Type III is related to hypothyroidism.

The pathophysiology of spontaneous OHSS associated with hypothyroidism is not studied well. The explanations given are (a) excessive estradiol via the 16-hydroxylation pathway instead of the normal 2-hydroxylation that has been demonstrated in hypothyroid patients. Excessive gonadotropin release, due to decreased feedback regulation caused by substitution of estradiol by the less potent estradiol, would result in spontaneous OHSS in those subjects;^[16] (b) High levels of thyroid stimulating hormone can directly stimulate ovaries in women with hypothyroidism and can cause ovarian hyperstimulation.^[5]

Mutations in the FSH receptor (FSHR) could be activating, leading to a predisposition to OHSS, or inactivating, resulting in sterility due to poor ovarian response to gonadotropins. Polymorphisms of FSHR have been investigated and about 744 single nucleotide polymorphisms have been identified in the FSHR gene, of which only eight are located in the coding region, exons, with the rest being intronic. Ovarian response is dependent on the FSHR genotype. Clinical studies on the p.N680S polymorphism of the FSHR gene have demonstrated the homozygous Ser/Ser variant to be less sensitive to endogenous or exogenous FSH in terms of oestradiol production. Polymorphism of the FSHR, Ser680Asn, in the FSHR gene is a predictor of the severity of symptoms in patients who develop OHSS.^[17,18]

Activating mutations of the FSHR gene that cause ovarian hyper-responsiveness to circulating FSH or even cross-responsiveness of FSHR to hormones having a structure similar to FSH, such as hCG or TSH^[19] hCG/LH receptor gene mutation claimed increased response to normal hCG levels and hence ovarian hyper responsiveness because of this mutation.^[20]

Unlike in iatrogenic OHSS, in spontaneous OHSS extravascular fluid retention may not occur and usually a hemodilution rather than hemoconcentration is seen as in this case (the blood picture showed anemia instead of hemoconcentration Table 1) and this may be due to the difference in the etiopathogenesis of iatrogenic and spontaneous OHSS. Again if, the spontaneous OHSS is due to high level of hCG concentration as in multiple gestation and trophoblastic disease then as in iatrogenic OHSS extra vascular fluid retention is common, raising the suspicion of difference in clinical presentation and pathogenesis according to the etiology. It is important to diagnose and manage spontaneous OHSS timely to prevent the occurrence of severe complication. Early diagnosis and appropriate treatment will avoid further complications. The OHSS is managed according to the degree of severity.

Hyperstimulated ovaries release a number of vasoactive mediators under the influence of hCG. These include vascular endothelial growth factor and several pro-inflammatory cytokines that interact to produce the characteristic pathophysiology of OHSS. This is marked by increased capillary permeability, leakage of fluid from the vasculature, third space fluid accumulation and intravascular dehydration.^[21]

Table 1: Blood analysis was performed at 9 and 20 weeks of gestation were as follows

Laboratory parameters	Report at (9 weeks of gestation)	Report at (20 weeks of gestation)
Hemoglobin%	9.6 Gm	10.8 Gm
Total leucocyte count	4000/cubic mm	7800/cubic mm
Platelet count	150000/cubic mm	195000/cubic mm
ESR	1 h: 57 mm	1 h: 16 mm
Peripheral smear	RBCs: Reduced in number and are normocytic and normochromic in appearance, WBCs: Normal in number and distribution, platelets: Adequate in number with normal morphological appearance, immature cells: No immature cells or atypical cells are seen, parasites: No malarial parasites or haemoparasites are observed	
Serom beta HCG level	181,264.20 mIU/ml	-
TSH (serum immunoassay)	150 µIU/ml	3.72 µIU/ml
Serum creatinine%	0.9 mg	0.8 mg
Total bilirubin%	0.6 mg	0.5 mg
SGPT	27 IU/L	24 IU/L
Total protein%	6.6 g	6.4 g
Albumin%	3.9 g	3.8 g

RBCs=Red blood cell; WBCs=White blood cell; ESR=Erythrocyte sedimentation rate; TSH=Thyroid stimulating hormone; SGPT=Serum glutamic pyruvate transaminase; HCG=Human chorionic gonadotropin



Figure 1: Transvaginal ultrasonography showing bilateral multilocular ovarian cystic masses with spontaneous ovarian hyperstimulation, spontaneously conceived singleton pregnancy at 9 weeks

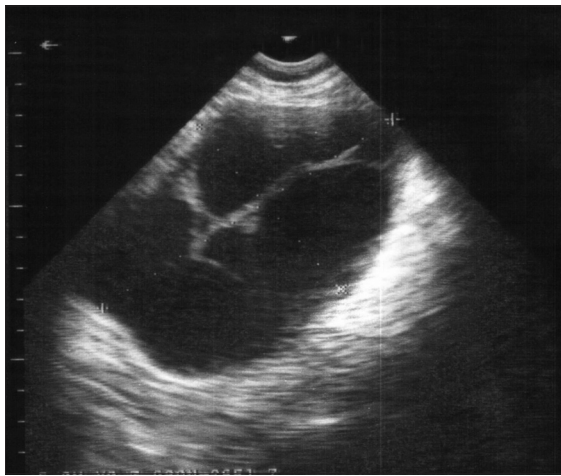


Figure 2: Hyperstimulated right ovary

Olatunbosun *et al.*,^[22] in 1996 reported a case of spontaneous OHSS in a patient with polycystic ovarian disease, who experienced severe spontaneous OHSS in four consecutive singleton pregnancies and achieved live births in two of the pregnancies. This was the third reported case of spontaneous OHSS associated with pregnancy and the first to result in live births. Ahmed Kamel^[1] reported a case of spontaneous OHSS in a woman, who presented in the second trimester of her first pregnancy with persistent abdominal pains, shortness of breath, vomiting, and diarrhea and the author stressed the importance of a thorough evaluation of all women who present with acute abdomen and ovarian masses during pregnancy as even though the condition is extremely rare, it can be lethal in its severe form if not timely diagnosed. Cardoso^[2] reported a case of naturally conceived pregnancy associated with spontaneous OHSS and primary hypothyroidism where TSH level and ovarian size returned to normal at 24 weeks of gestation. Edwards-Silva *et al.*^[3] reported a

case of pregnancy with spontaneous OHSS syndrome, uncontrolled hypothyroidism, elevated hCG, deep vein thrombosis, and Rh isoimmunization and conservatively managed with levothyroxine and heparin and noted regression of the ovaries by 22 weeks of gestation after adequate thyroid repletion and delivered a non-hydropic preterm baby at 35 weeks of gestation.

It is imperative that all health care providers, including gynecologists, surgeons and physicians should consider hypothyroidism and other endocrine disorders in the differential diagnosis of adult females presenting with multicystic ovarian tumors to avoid unnecessary and catastrophic ovarian resection.^[8]

In non-pregnant subjects, the clinical presentation of spontaneous OHSS ascites, ovarian enlargement and pleural effusion may misdiagnose this condition as advanced ovarian malignancy and may ended up in exploratory laparotomy. Hence, proper evaluation and correct diagnosis are important for the prevention of mismanagement.

Rarity of this condition may also be due to misdiagnosis and by missing the diagnosis that can result in mismanagement or severe complications of this condition.

REFERENCES

1. Ahmed Kamel RM. Spontaneous ovarian hyperstimulation syndrome in a naturally conceived singleton pregnancy. *Fertil Steril* 2010;94:351.e1-4.
2. Cardoso CG, Graça LM, Dias T, Clode N, Soares L. Spontaneous ovarian hyperstimulation and primary hypothyroidism with a naturally conceived pregnancy. *Obstet Gynecol* 1999;93:809-11.
3. Edwards-Silva RN, Han CS, Hoang Y, Kao LC. Spontaneous ovarian hyperstimulation in a naturally conceived pregnancy with uncontrolled hypothyroidism. *Obstet Gynecol* 2008;111:498-501.
4. Yamashita Y, Kawamura T, Fujikawa R, Mochizuki H, Okubo M, Arita K. Regression of both pituitary and ovarian cysts after administration of thyroid hormone in a case of primary hypothyroidism. *Intern Med* 2001;40:751-5.
5. Taher BM, Ghariabeh RA, Jarrah NS, Hadidy AM, Radaideh AM, Ajlouni KM. Spontaneous ovarian hyperstimulation syndrome caused by hypothyroidism in an adult. *Eur J Obstet Gynecol Reprod Biol* 2004;112:107-9.
6. Bassam T, Ajlouni K. A case of ovarian enlargement in severe primary hypothyroidism and review of the literature. *Ann Saudi Med* 2006;26:66-8.
7. Kubota K, Itho M, Kishi H, Igarashi S, Minegishi T. Primary hypothyroidism presenting as multiple ovarian cysts in an adult woman: A case report. *Gynecol Endocrinol* 2008;24:586-9.
8. Shu J, Xing L, Zhang L, Fang S, Huang H. Ignored adult primary hypothyroidism presenting chiefly with persistent ovarian cysts: A need for increased awareness. *Reprod Biol Endocrinol* 2011;9:119.
9. Panico A, Lupoli GA, Fonderico F, Colarusso S, Marciello F, Poggiano MR, *et al.* Multiple ovarian cysts in a young girl with severe hypothyroidism. *Thyroid* 2007;17:1289-93.
10. Gordon CM, Austin DJ, Radovick S, Laufer MR. Primary hypothyroidism presenting as severe vaginal bleeding in a prepubertal girl. *J Pediatr Adolesc Gynecol* 1997;10:35-8.

11. Ryan GL, Feng X, d'Alva CB, Zhang M, Van Voorhis BJ, Pinto EM, *et al.* Evaluating the roles of follicle-stimulating hormone receptor polymorphisms in gonadal hyperstimulation associated with severe juvenile primary hypothyroidism. *J Clin Endocrinol Metab* 2007;92:2312-7.
12. Browne LP, Boswell HB, Crotty EJ, O'Hara SM, Birkemeier KL, Guillerman RP. Van Wyk and Grumbach syndrome revisited: Imaging and clinical findings in pre- and postpubertal girls. *Pediatr Radiol* 2008;38:538-42.
13. 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.
14. Zalel Y, Katz Z, Caspi B, Ben-Hur H, Dgani R, Insler V. Spontaneous ovarian hyperstimulation syndrome concomitant with spontaneous pregnancy in a woman with polycystic ovary disease. *Am J Obstet Gynecol* 1992;167:122-4.
15. De Leener A, Montanelli L, Van Durme J, Chae H, Smits G, Vassart G, *et al.* Presence and absence of follicle-stimulating hormone receptor mutations provide some insights into spontaneous ovarian hyperstimulation syndrome physiopathology. *J Clin Endocrinol Metab* 2006;91:555-62.
16. Rotmensch S, Scommegna A. Spontaneous ovarian hyperstimulation syndrome associated with hypothyroidism. *Am J Obstet Gynecol* 1989;160:1220-2.
17. Rizk B. Symposium: Update on prediction and management of OHSS. Genetics of ovarian hyperstimulation syndrome. *Reprod Biomed Online* 2009;19:14-27.
18. Vassart G, Pardo L, Costagliola S. A molecular dissection of the glycoprotein hormone receptors. *Trends Biochem Sci* 2004;29:119-26.
19. Lussiana C, Guani B, Restagno G, Rovei V, Menato G, Revelli A, *et al.* Ovarian hyper-stimulation syndrome after spontaneous conception. *Gynecol Endocrinol* 2009;25:455-9.
20. Akerman FM, Lei Z, Rao CV, Nakajima ST. A case of spontaneous ovarian hyperstimulation syndrome with a potential mutation in the hCG/LH receptor gene. *Fertil Steril* 2000;74:403-4.
21. Alper MM, Smith LP, Sills ES. Ovarian hyperstimulation syndrome: Current views on pathophysiology, risk factors, prevention, and management. *J Exp Clin Assist Reprod* 2009;6:3.
22. Olatunbosun OA, Gilliland B, Brydon LA, Chizen DR, Pierson RA. Spontaneous ovarian hyperstimulation syndrome in four consecutive pregnancies. *Clin Exp Obstet Gynecol* 1996;23:127-32.

How to cite this article: Sridev S, Barathan S. Case report on spontaneous ovarian hyperstimulation syndrome following natural conception associated with primary hypothyroidism. *J Hum Reprod Sci* 2013;6:158-61.

Source of Support: Nil, **Conflict of Interest:** None declared.

Staying in touch with the journal

1) Table of Contents (TOC) email alert

Receive an email alert containing the TOC when a new complete issue of the journal is made available online. To register for TOC alerts go to www.jhrsonline.org/signup.asp.

2) RSS feeds

Really Simple Syndication (RSS) helps you to get alerts on new publication right on your desktop without going to the journal's website. You need a software (e.g. RSSReader, Feed Demon, FeedReader, My Yahoo!, NewsGator and NewzCrawler) to get advantage of this tool. RSS feeds can also be read through FireFox or Microsoft Outlook 2007. Once any of these small (and mostly free) software is installed, add www.jhrsonline.org/rssfeed.asp as one of the feeds.