MAR Gynecology & Urology (2025) 8:3

Case Report

A Very Rare Presentation of Spontanous Ovarian Hyperstimulation Syndrome at Term Pregnancy in Early Labor. Case Report with Narrative Review of Literature

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Received: 21 March 2025

Published: 29 March 2025

Introduction

Ovarian hyper stimulation syndrome ((OHSS)) is a rare, iatrogenic, life-threatening, complication of ovulation induction with various types of infertility treatment. Spontaneous ovarian hyper stimulation ((s OHSS)) which occur without ovulation induction /with or without pregnancy is extremely rare.

OHSS was first described in 1943, (1). The first spontaneous OHSS was described by Van Wyk and Grumbach in young girl with combination of multicystic ovaries, juvenile hypothyroidism and precocious puberty in 1960, (2) Rotmensch and Scommegna describe the first case of spontaneous OHSS in hypothyroid woman in 1989. (3) In 1996 Olatunbosun et al. first reported a case of severe spontaneous OHSS associated with pregnancy and polycystic ovarian disease to result in live birth.(4)

Although OHSS is predominantly an iatrogenic condition, there are reports of it occurring in association with: Multiple pregnancies, Fetal and placental triploidy, Hydatiform moles, Hypothyroidism, Polycystic ovary syndrome (PCOS) , and high levels of Human chorionic gonadotropins (hCG) or anti mullerian hormone (AMH). s OHSS was observed also in young girls and non-pregnant women. (2-14)

The etiology & pathogenesis of spontaneous OHSS is still not clear. The observations of etiopathogenesis of OHSS explained that the hyperstimulated ovaries release a number of vasoactive mediators under the influence of hCG. These include: vascular endothelial growth factor and several proinflammatory 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.(2,15) This may cause hypoalbuminaemia, haemoconcentration, electrolyte imbalance, decreased renal perfusion and oliguria, ascites, pleural/pericardial effusions, which may importantly precipitate significant morbidity and mortality from thrombosis, renal, liver and respiratory failure (ARDS). Ovarian enlargement also creates risk of torsion and cyst rupture. (16,17)

Royal College of Obstetricians and Gynecologists in 2006. Proposed a classification of severity OHSS as: Mild, Moderate, Severe and Critical based on the clinical criteria. The incidence of Mild, Moderate and Severe varies respectively between 5–10%, 3-6%, 0.2–1.2% of cycles in anovulatory women treated with different preparations for induction of ovulation .(18)

Spontaneous OHSS is likely to occur at 8-14 weeks of gestation, while iatrogenic OHSS usually occurs earlier at 3-8 weeks of gestation. Iatrogenic OHSS is self-limiting and usually resolves spontaneously within several days, but may persist for a longer duration, particularly in treatment cycles where conception occurs. (10-15,17)

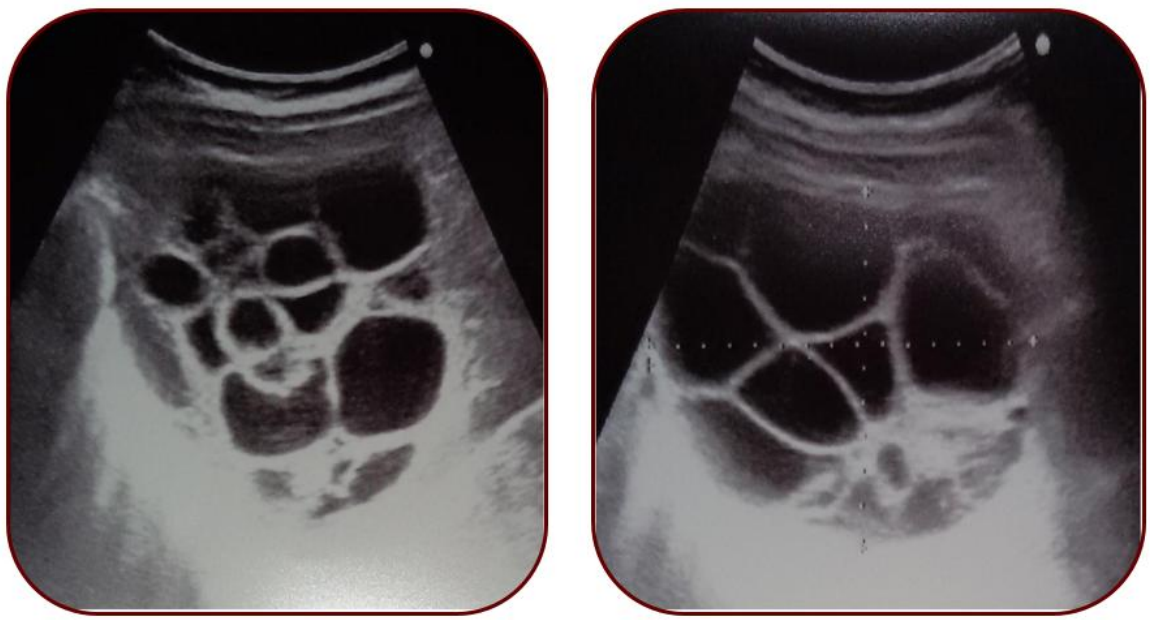
Tokmak Aytekin et al., 2015; first publish a case of spontaneous ovarian hyperstimulation late in a term

pregnancy. (19) The aim of this study is to report a second case of very rare spontaneous OHSS at term pregnancy and the first one who presents during labor, and to offer a narrative review of the literature in the context of s OHSS with term delivery.

Case Report

A 20 year old primi-gravida, at 38 weeks with history of regular menstrual cycle, married for 11 months, has no significant past medical or surgical history. She conceived spontaneously and denied having ever taken any ovulation induction drugs. She was observed up until 36 weeks of gestation, and her pregnancy was normal. She presented to my clinic on 11th June 2014, during the 38th week of gestation with complaints of abdominal pain, abdominal distention and nausea. General examination: the patient was young and healthy with normal average weight and height, and normal vital signs. Abdominal examination: the abdomen was distended tender and tense, with irregular contour lateral to the uterine fundus, fundal height is 34cm, longitudinal lie and cephalic presentation, contractions 2/10'/20-25" and active fetal heart rates 150/mint. By pelvic examination: the cervix was opened 2 ½ cm, effaced 50%, membrane intact, vertex presentation, at zero station. Ultrasound findings: Single alive fetus cephalic presentation, BPD corresponds to 36th weeks, active FHR=145bpm, adequate amniotic fluid, fundal mature placenta, and EFW=2750gram.

The right ovary measured 8.6 x 8.4 cm, with multiple cysts of variable sizes.The Left ovary measured 9.0 x 6.1 cm, with multiple cysts of variable sizes. No ascites were detected.



THE RIGHT OVARY THE LEFT OVARY

Fig 1

Management

A diagnosis of moderate spontaneous OHSS at term pregnancy in labor was done. The patient referred to maternity hospital for delivery . Laboratory testing revealed normal CBC values and normal liver and renal functions. The patient was managed conservatively and followed for labor progress as usual. At 7am next morning, she has spontaneous normal vaginal delivery, of a healthy male baby weighed 2700 grams. The patient was discharged the second day post-delivery without problems. The ovaries returned to normal 4 weeks after delivery.

Discussion

Spontaneous ovarian hyperstimulation is extremely rare in naturally conceived pregnancies. In the literatures s OHSS was observed with early onset in the first trimester. Patil H. et al reports a rare case of late onset severe s OHSS in the second trimester of pregnancy.(20) s OHSS in a term pregnancy is extremely rare.

Tokmak Aytekin et al publish the first and the only one reported case in the literature.(19) In this study OHSS has seen in a singleton spontaneous gestation late at term pregnancy and during early stages of labor.

The diagnosis of OHSS is made on clinical grounds, ultrasound play an important role in the detection of multi cystic ovaries and associated third space fluid collection. In Table (1), the proposed RCOG classification of severity of OHSS, In its most severe form, there is a tremendous increase in ovarian size (greater than 10 cm increase in diameter, with attendant abdominal distention, ascites, pleural effusion, and decreased intravascular volume. Rarely, OHSS may be associated with life threatening complications, including renal failure, acute respiratory distress, hemorrhage from ovarian rupture and thromboembolism. Deaths after OHSS have been reported (ESHRE EIM Annual reports). (16-18)

Table (1): Proposed RCOG Classification of Severity of OHSS

Category	Features
Mild	Mild abdominal pain Abdominal bloating Ovarian size usually < 8 cm

Moderate	Moderate abdominal pain Nausea +/- vomiting Ultrasound evidence of ascites Ovarian size 8-12 cm
Severe	Clinical ascites (± hydrothorax) Oliguria(<300 ml/day or <30ml/hour Haemoconcentration (Haematocrit > 45%) Hypo-osmolality (osmolality <282 mosm/kg) Hyperkalemia (potassium >5 mmol/L) Hypoproteinaemia, (serum albumin < 35g/L) Ovarian size > 12 cm
Critical	Tense ascites/ large hydrothorax Haematocrit > 55% White cell count > 25 000/ml Oligo/anuria Thromboembolism Acute respiratory distress syndrome

Treatment of mild and moderate OHSS is conservative. Treatment of severe form aimed at maintaining intravascular volume and preventing hemoconcentration and hypovolemia and their adverse consequences on coagulation and kidney function.(8)

OHSS is very rare in a term pregnancy because of early onset of a disease and/ or negative pregnancy outcome. Although pregnancy outcome were not studied well in patients with this rare syndrome, there are some published articles of spontaneous OHSS with negative pregnancy outcome like abortion; missed or induced, stillbirth and spontaneous or iatrogenic preterm delivery due to severe maternal complications. (4,8,21,22)

A narrative literature review of spontaneous OHSS publications according to various explanations of etiopathogesis and underlying pathology or risk factor which continued to term delivery are present in this discussion.

Some authors report s OHSS with unknown etiology and unexplained pathophysiology in patients with term delivery despite early onset of a disease. (23-32) Table (2); Summarize the published cases and define the gestational age at onset of s OHSS, severity of symptoms, type of management and gestational age at regression of ovaries then the gestational age at pregnancy outcome. it is shown that all reported early onset of s OHSS and ovarian regression by the end of first or second trimester.

Ayhan et al (1996) also first describe a case of severe s OHSS at 12th week gestation continued to term delivery, and treated surgically by cyst excision and aspiration of ascites, the ovaries regress 7 days post-operative.(23)

Amini A. et al. (2000) describe severe s OHSS early at 7th week of pregnancy , managed conservatively and ended successfully at term. (24)

Chae et al (2001), Shergill S.et al. (2005), Cepni et al, (2006), Temur L.et al (2014), have patients with severe s OHSS diagnosed at 10th ,12th +5,11th and 10th weeks of gestations respectively , treated conservatively and symptomatically and their pregnancies ended with successful term deliveries.(25-28)

Tokmak A. et al. (2015), published a first case of moderate s OHSS at 37th weeks of gestation, in a patient previously healthy and was observed up in to 35th week. She managed conservatively, and delivered spontaneously at 40 weeks by CS due to fetal macrosomia. Ovarian cysts (ovarian size 13.6×11.2cm) were drilled with electrocautry during CS. Her ovaries return to normal size after two weeks. (19).

Table (2): Overview of the literatures describing cases of s OHSS with term delivery with unknown etiology & pathogenesis.

Author	First diagnosis	Severity of OHSS	Management	Regression of Ovaries	Result
Kantarci S. et al. (2021)	10th week	Moderate	Conservative	At 6th week post delivery	**Delivery by CS at 39 weeks/ PET**
Stolorz k. et al. (2016)	11th week	Moderate	Conservative	At 14th week	**Delivery at 39 weeks**
Fábio Roberto Cabar (2016)	12th	Severe	Intravascular human albumin for 3 days, furosemide (40mg/day) and prophylactic dose of enoxaparin.	Six weeks after delivery	**Delivery at 38+5 weeks**
Ainsworth A. et al. (2016).	8th week	Severe	Conservative, Thoracocentesis	At 11th week	**Induced at 39, +7 weeks**
Same patient	7th week	Severe	Supportive therapy in ICU	At 10th week	**Delivery at 37 weeks**
Osaikhuwuomwan et al. (2016)	10thweek	Severe	Symptomatic	At 26th week	**Delivery at 39 weeks**
Tokmak A. et al.(2015)	37th week	Moderate	Conservative Ovaries were drilled during CS	Two weeks after birth	**Delivery at 39 weeks**

Temur I. et al. (2014)	10^{th} week	Severe	Conservative respiratory physiotherapy, Thoracocentesis	At 14^{th} week	**Delivery at 37 weeks**
Cepni et al. (2006)	11^{th} week	Severe	Symptomatic	At 23^{rd} week	**Delivery at term**
Shergill S.et al. (2005)	$12,5^{th}$ week	Severe	Supportive therapy	At 26^{th} week	**Delivery at 40 weeks**
Chae et al. (2001)	10^{th} week	Severe	Symptomatic, plasma expanders	Four weeks after delivery	**Delivery at 41+4 weeks**
Amini A. et al. (2000)	7^{th} week	Severe	Conservative, paracentesis,	At 20^{th} week	**Delivery at 38 weeks**
Ayhan A. et al. (1996)	12^{th} week	Severe	Laparotomy for Cyst excision and aspiration of ascites.	7 days post-operative	**Delivery at term**

Osaikhuwuomwan et al. (2016), and Ainsworth A. et al.t al.(2016) report patients with term deliveries after severe s OHSS in first trimester.(29,30).

Fábio Roberto Cabar (2016) report patients with severe s OHSS in first trimester, managed with Intravascular human albumin for 3 days, furosemide (40mg/day) and prophylactic dose of enoxaparin. and ended with successful term delivery at 38+5 weeks. (31).

Stolorz K. et al. (2016), and Kantarci S. et al. (2021), have diagnosed their patients with moderate s OHSS in the first trimester, managed conservatively to end with term deliveries.(32,33)

Certain illnesses like hypothyroidism, hydatidiform mole, or multiple pregnancies, which come along with elevated HCG concentrations, can theoretically cause spontaneous OHSS (Ludwig et al., 1998; Tanaka et al., 2001;Taher et al., 2004;Guvenal et al., 2006). (6,34-36)

The explanation of the pathophysiology of s OHSS associated with hypothyroidism given are: (a) excessive estriol 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 estriol, would result in spontaneous OHSS in those subjects;(3) (b) High levels of thyroid stimulating hormone can directly stimulate ovaries in women with hypothyroidism and can cause ovarian hyperstimulation.(35)

Early recognition and stabilization of the thyroid gland in patients with hypothyroidism can improve clinical and radiological findings of s OHSS and results in successful pregnancy outcome.

Table (3). Presents publications of s OHSS associated with hypothyroidism and polycystic ovary (PCOS), which progressed to term delivery.

Olatunbosun et al. (1996) first describe four recurrent s OHSS in a patient with PCOS; which managed conservatively and observed up to term delivery and the ovaries return to normal after term live birth in two different pregnancies of the same patient. one of the other two pregnancies end in still birth at term and the other end in induced abortion due to the severity of symptoms.(4)

Zalel and colleagues describe a case of OHSS associated with spontaneous pregnancy in a woman with polycystic ovarian disease. (37)

Rohatgi B. et al. (2017) published a case of s OHSS with PCOS diagnosed early at 4th week and ends in successive term delivery by cesarean section due to labor non progress.(38)

Dieterich M. et al. (2010) reported a patient with Epilepsy, Hypothyroidism developed moderate s OHSS at 10th week gestation and managed conservatively with thyroid drugs and paracentasis. she delivered at 39 weeks. And s OHSS diagnosed to be due to positive FSHR mutation.(39)

Guvenal et al. (2006), Borna and Nasery et al. (2007), Akbay E. et al. (2010). Sridev S. et al (2013). Souza Lucas. et al. (2021) reported s OHSS in patients with Hypothyroidism treated by stabilization of thyroid gland with levothyroxine and delivered at term. the ovarian regression was variable some patients have late regression, few weeks to months after delivery.(36,40-43).

Table (3): Overview of the literatures describing cases of s OHSS with term delivery having Hypothyroidism / polycystic ovary

Author	Etiology & pathogenesis	First diagnosis of OHSS	Severity of OHSS	Management	Regression of Ovaries	Result
Souza Lucas. et al. (2021)	Hypothyroidism	13th week	Moderate	Levothyroxine	8 months after delivery	**Delivery at 37 weeks**
Rohatgi B. et al. (2017)	Polycystic ovary syndrome	4th week	Mild	conservative	----------	**Delivery by CS at term /non progress.**
Sridev S. et al (2013)	Hypothyroidism	9th week	Mild	Levothyroxine	At 20th week	**Delivery at 39 weeks**
Dieterich M. et al. (2010)	FSH Mutation Epilepsy	10th week	Moderate	Conservative , Levothyroxi	----------	**Delivery at 39 weeks**

	Hypothroidism			ne , Paracentesis		
Akbay E. et al. (2010)	Hypothyroidism	10th week	Mild	Levothyroxine	3 months postpartum	**Delivery at 38 weeks**
Same patient		12th week	Mild	Levothyroxine	AT 8th week postpartum	**Delivery at 38 weeks**
Borna and Nasery et al. (2007)	Hypothyroidism	20th week	Mild	Levothyroxine , aspiration of cysts during CS	At 10th week postpartum	**Delivery by CS at 38TH week/ Breech**
Guvenal et al. (2006)	Hypothyroidism	----------	----------	Levothyroxine	----------	**Delivery at term**
Olatunbosun et al. (1996)	Polycystic ovary syndrome	8th week	Severe	Observation	At 8 weeks postpartum	**Delivery at term**
1994		14th week	Mild	Observation	----------	**Stillbirth at 41+5 weeks**
1989		13th week	Mild	Observation	Postpartum	**Delivery at term**
1987 The same patient with recurrent s OHSS						

Spontaneous OHSS can be associated with hormone-producing tumors or endocrinological dysfunctions. HCG is thought to play a crucial role in the development of the syndrome. There are many studies explained the relation between elevated levels of B hCG and OHSS Table (4).

Suzuki (2004) have diagnosed three different pregnancies with s OHSS and elevated serum level of B hCG in two sisters and positive family history.(44)

R.Haimov-Kochman et al.(2004), Oztekin, et a. (2006), Demirel E. et al, (2016), Juan Gui et al. (2019) and Rastin Z. et al. (2019) published their reports of s OHSS in first trimester pregnancies with elevated high levels of B hCG without any other underlying pathology, patients were managed conservatively, and ovarian regression occur during pregnancy by the first or second trimester.(45- 49).

Table (4): Overview of the literatures describing cases of s OHSS with term delivery related to HCG.

Author	Etiopathogenesis	First diagnosis of s OHSS	Severity of OHSS	Management	Regression of Ovaries	Result
Rastin Z.et al.(2019)	HCG=96,100 IU/L	8th week	Moderate	Conservative	At 18th week	**Delivery at 39 weeks**

Juan Gui et al. (2019)	HCG= >200,000 IU/L	12th +5 weeks	Severe	Conservative , Pleurocentesis	----------	**Delivery at 40 weeks**
Demirel E. et al. (2016)	HCG=630,631 IU/L	11th week	Severe	Conservative,	At 17th +6 week	**Delivery at 40 weeks**
Oztekin et al. (2006)	HCG=143,393 IU/L	10th week	Moderate	Symptomatic	At 20th week	**Delivery at 39 weeks**
R.Haimov-Kochman et al.(2004)	HCG= 137,100 IU/L	13th week	Moderate	Expectant	After 2 months	**Delivery at term**
Suzuki (2004) Same patient	HCG=89,000 IU/L	10th week	Severe	Conservative	At 13th + 4 week	**Delivery at 40 weeks**
Her sister		10th week	Mild	Conservative	----------	**Delivery at term**
Positive family history		11th week	Moderate	Conservative	----------	**Delivery at term**

Recent medical researches and studies explain the role of FSH receptors mutations in the pathogenesis of s OHSS, Mutations in the FSH receptor (FSHR) could be activated, leading to OHSS. 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. (49,50) hCG/LH receptor gene mutation claimed increased response to normal hCG levels and hence ovarian hyper responsiveness because of this mutation.(22)

Table (5) show studies of s OHSS due to follicle stimulating hormone receptors (FSHR) mutations. Smits et al. (2003) and Vasseur et al. (2003) describe for the first time a mutation in the FSHR as a cause of spontaneous OHSS. (51,52).

De Leener et al (2008), classified spontaneous OHSS in to three types based on the clinical presentation and FSH receptor mutation.(53) *Type I corresponds to the mutated FSHR cases.

* Type II corresponds to the spontaneous OHSS secondary to high levels of hCG. This type is probably the most frequently encountered. *Type III is related to hypothyroidism.

In some cases, a combination of supposed risk factors and simultaneous FSHR mutation might have led to s

OHSS, (Ludwig et al., 1998; Cardoso et al., 1999; Suzuki, 2004, Guvenal et al 2006;). (6,36,44,54)
There are four different FSHR mutations have been described in relation to s OHSS, Dieterich et al.(2008), De Leener et al. (2006), Montanelli et al. (2004), Vasseur et al. (2003), Smits et al. (2003).(39,51,53,55-57)
Literatures also report cases of recurrent s OHSS which end in a term delivery in patients with FSHR mutations, and positive family history and s OHSS have seen also in their sisters and relatives. Montanelli et al. (2004), Vassart et al. (2004), Guillaume Smits et al. (2003). (51,56,57).

Roperts et al.(2005) published a rare case of s OHSS in a pregnant woman due to FSH secreting pituitary adenoma, managed by transphenoidal resection of the adenoma and continue pregnancy to term.(58)

Yilmaz et al. (2016) reports another two successful term deliveries in patients with s OHSS and FSHR mutations. (59)

Table (5): Overview of the literatures describing cases of s OHSS with term delivery and FSHR Mutations.

		diagnosis of OHSS	OHSS	Ovaries		
Yilmaz E. et al. (2018)	FSH Mutation	12^{th} week	Moderate	Conservative	Postpartum	**Delivery at 38 weeks**
Another patient		10^{th} week	Moderate	Conservative	----------	**Delivery at 40 weeks**
Dieterich M. et al. (2010)	FSH Mutation Epilepsy Hypothroidism	10^{th} week	Moderate	Conservativ, Levothyroxine , Paracentesis	----------	**Delivery at 39 weeks**
De Leener et al (2006)	FSH Mutation	12^{th} week	Severe	Symptomatic	Postpartum	**Delivery at term**
Roperts et al (2005)	FSH secreting pituitary adenoma	----------	----------	Transsphenoidal resection of the adenoma	----------	**Delivery at term**
Montanelli et al. (2004)	FSH Mutation	10^{th} week	Mild	Conservative	----------	**Delivery at term**
Same		10^{th} week	Severe	Conservative	----------	**Delivery at 40 weeks**

patient Her sister Positive family history		11th week	Severe	Conservative	----------	**Delivery at term**
Vasseur et al (2003)	FSH Mutation	8th week	Severe	Conservative	----------	**Delivery at 38 week**
Same patient Positive family history		8th week	Moderate	Conservative	After delivery	**Delivery at term**
Guillaume Smits et al. (2003) Recurrent in 4 pregnancies of the same patient. 3 of ,them reach term	FSH Mutation	13th week	Mild	Untreated	8 weeks postpartum	**Delivery at term.**
		14th week	Severe	Untreated	12 weeks postpartum	**Intrauterine death at 41+5 week**
		8th week	Severe	Paracentesis	8 weeks postpartum	**Delivery at term**

In cases of spontaneous OHSS with normal HCG concentrations and no pathophysiological correlation, a FSHR mutation is now a possible explanation for developing spontaneous OHSS. In general, OHSS occurs at the beginning of pregnancy and rarely continues beyond the first trimester.

It is extremely rare to find s OHSS developed late in a term pregnancy as observed in previous studies, the course of pregnancy and obstetrical complications in women with OHSS did not differ from that of the normal patients.

Up to my knowledge Tokmak A. et al. (2015), was the first one who report a first case of s OHSS at 37th weeks of gestation and delivered at 40 weeks by CS. Her ovaries return to normal size after two weeks. By literature review it was the only one published case of s OHSS in a term pregnancy. This case is more interested that she is a case of spontaneous OHSS in a healthy primigravida with no associated risk factor other than her young age, and first presentation of s OHSS late in a term pregnancy during early stages of spontaneous labor.

Conclusion

Spontaneous OHSS during term pregnancy is an extremely rare condition. There are only one reported case of spontaneous OHSS described late in pregnancy, and no any case with s OHSS, discovered late in term

pregnancy and / or during labor. it is necessary to evaluate all pregnant women mainly those with enlarged ovaries for the possibility of spontaneous OHSS as this rare entity may occur in natural pregnancy. Early identification and appropriate supportive therapy in a patient with OHSS can improve the quality of life and pregnancy outcome. If left untreated, OHSS can result in serious health complications and even death. Ultrasonography is a good tool for diagnosis and follow up of OHSS.

Conflict of Interest:

There is no conflict of interests, be it financial or in any other form.

References

1. Michael M, Alper, Laura P, Smith, Eric Scott Sills, et al. Ovarian Hyperstimulation Syndrome : Current Views on Pathophysiology, Risk Factors, Prevention, and Management. J Exp Clin Assist Reprod.2009:6:3. [PMC free article] [PubMed.]

2. Van Wyk JJ, Grumbach MM. Syndrome of precocious menstruation and galactorrhea in juvenile hypothyroidism: an example of hormonal overlap in pituatory feedback. J Paediatr 1960;57:20. Available on: http://refhub.elsevier.com/S2666-3341(21)00082-9/sref3 .

3. Rotmensch S, Scommegna A. Spontaneous ovarian hyperstimulation syndrome associated with hypothyroidism. Am J Obstet Gynecol 1989;160:1220-2 .

4. 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.

5. Ahmed Kamel RM. Spontaneous ovarian hyperstimuation syndrome in a naturally conceived singleton pregnancy. Fertil Steril 2010;94:351.e1-4.

6. Ludwig M, Gembruch U, Bauer O, and Diedrich K. Ovarian hyperstimulation syndrome in spontaneous pregnancy(OHSS)with fetal and placental triploidy: information about the general pathophysiology of OHSS. European Society for Human Reproduction and Embryology. Human Reproduction vol.13. no 8, pp. 2082-7, 1998.

7. Agrawal NR, Gupta G, Verma K, Varyani N. Spontaneous ovarian hyperstimulation syndrome in a triplet pregnancy. Case reports in critical care:2012, article ID 189705. Available on: doi:10.1155/2012/189705 .

8. Rachad M, Chaara H, Fdili F, Bouguern H, Melhouf A. Ovarian hyperstimulation syndrome in spontaneous pregnancy with invasive mole: report of a case. N Afr Med J,2011;9:23.

9. Peluso C, Fonesca 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 Physiology Biochem 35:1401-12

10. 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 hyperstimualtion syndrome. Am J Transl Res7:1925-38.

11. Wang L, Li H, Ai J, Zhang H, Zhao Y.(2015). Possible involvement of single nucleotide polymorphisms in antimullerian hormone signaling pathway in the pathogenesis of early OHSS in Han Chinese woman. Int J Clin Exp Pathol 8;9552-9.

12. Ileanchezhian S, Mohan SV, Ramachandran R, Babu SR. Spontaneous ovarian hyperstimulation syndrome with primary hypothyroidism: Imaging a rare entity, Radiology case reports: (online)2015;10(1);1050.

13. Goel Alka. Primary hypothyroidism presenting as Spontaneous ovarian hyperstimulation. Obstet Gynecology Int J 2017,7(1):00236.

14. Chai W, He H, Li Fei, Zhang W, He Chao. Spontaneous ovarian hyperstimulation in nonpregnant female patient: a case report and literature review. Journal OF International Medical Research2020, 48(9): 1-8.

15. 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.

16. Clinical practice guidelines. Ovarian Hyperstimulation syndrome (OHSS) Diagnosis and Management. Institute of Obstetrician and Gynecologists, Royal College of Physicians of Ireland and Directorate of Strategy and Clinical Programs, Health Service Executive Version1.0 April 2012 Guideline No.9 Revision date April 2014.

17. Braat DD, Schutte JM, Bernardus RE, Mooij TM, van Leeuwen FE. Maternal death related to IVF in the Netherlands 1984-2004. Hum Reprod 2010; 25:1782-6.

18. Royal College of Obstetricians and Gynecologists. The Management of Ovarian Hyperstimulation syndrome, Green Top Guideline No. 5, February 2016.

19. Tokmak A, Guzel A. Kangal K, Yalinkaya A. Spontaneous Ovarian Hyperstimulation Syndrome in a Term Pregnancy. A Case Report. Cukurova Medical Journal 2015: 40(3); 623- 6.

20. Patil H.N. Roy R. Pal Raja. Spontaneous late onset OHSS in singleton pregnancy in second trimester: A Rare Case, the journal of obstetrics and gynecology 2015;65(1):50-3.

21. Halim B, Lubis HP, Amalia T, Ovarian hyperstimulation syndrome in spontaneous pregnancy with sacrococcygeal teratoma complicated by maternal mirror syndrome: A comorbidity. Middle East Fertility Society Journal 2016; 21,277-80.

22. 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. Fertility and Sterility2000,74(2.(

23. Ayhan A, Tuncer Z.S, and Aksu. Ovarian hyperstimulation syndrome associated with spontaneous

pregnancy. A Case Report. Human Reproduction vol.11. no 8, pp. 1600-1601, 1995.

24. Amini A MD, Kheshti F. MD, Badakhsh MD. ovarian hyperstimulation syndrome (OHSS) in a singleton pregnancy: A Case Report. SID, Arhive of Iranian Medicine vol 203, 21/08/2005.

25. Chae Hee-Dong, et al. ovarian hyperstimulation syndrome complicating a spontaneous singleton pregnancy: A Case Report. Journal of Assisted Reproduction and Genetics, vol. 18, no. 2, 2001.

26. Shergill SK, Kaur S, Jain S. Spontaneous ovarian hyperstimulation in singleton gestation. J Obstet Gynecol India Vol. 55, no.4, July/ August 2005, pp. 369-71.

27. Cepni, I., Erkan, S, et al. 2006. Spontaneous ovarian hyperstimulation syndrome presenting with acute abdomen. J. Postgrad. Med. 52,154-5.

28. Temur I, Bouzkurt M, Gencdal S, Karasu Y, Bozkurt DK, Pasaoglu H, Ulker K, Dede S. Severe ovarian hyperstimulation in spontaneous pregnancy, Proceeding in Obstetrics and Gynecology, 2014;4 (3): Article 9 [6p.]. Available from: http://ir.uiowa.edu/pog./

29. Osaikhuwuomwan James A, Osemwenkha Abieyuwa P, ovarian hyperstimulation syndrome in a spontaneous pregnancy: A potential for missed diagnosis; Niger Med J, 2016 Jan:Feb; 57
(1): 74-6.

30. Ainsworth A, Khan Z, Jensen J (2016) An Idiopathic Case of Recurrent Spontaneous Ovarian Hyper Stimulation Syndrome. Obstet Gynecol Cases Rev 3:081

31. Fábio Roberto Cabar (2016). Ovarian hyperstimulation syndrome in a spontaneous singleton pregnancy, Case report. einstein. 2016;14(2):231-4

32. Stolorz K, Nowosielski K, Wjodarz IU, Sodowska P, Sodowska k (2016) Ovarian hyperstimulation syndrome in spontaneous pregnancy. J Gynecol Res Obstet 2 (1) 005-009. doi: http://dx.doi.org/10.7352/jgro.000007.

33. KantarcıS, AkpakYK, ÖztürkB, OralS, EmreA, İleriA,et al. Development and management of ovarian hyperstimulation syndrome in spontaneous singleton pregnancy. Int J Reprod Contracept Obstet Gynecol 2021;10:3954-7.

34. Tanaka, Y. Yanagihara, T. et al Naturally conceived twin pregnancy with hyperreactio luteinalis, causing hyperandrogenism and maternal virilization. Acta Obstet Gynecol. Scand. 80, 277-8.

35. 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.

36. Guvenal F, Guvenal T, Timuroglu Y, Timuroglu T, Cetin M. Spontaneous ovarian hyperstimulation like reaction caused by primary hypothyroidism. Acta Obstet Gynecol Scand 2006;85:124-5

37. 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.

38. Rohatgi TB, Buckshee K. A unique Variant of spontaneous ovarian hyperstimulation syndrome: case report. International Journal of Reproduction, Contraception, Obstetrics And Gynecology, Vol 6, No 9 (2017). http://www.ijrcog.org/index.

39. Dieterich M, Bolz M, Reimer T, Costagliola S, Gerber B. Two different entities of spontaneous ovarian hyperstimulation In a woman with FSH receptor mutation. Reprod Biomed Online 2010,20:751-8. http://refhub.elsevier.com/S2666-3341(21)00082-9/sref51

40. Borna S, Nasry A. Spontaneous ovarian hyperstimulation syndrome in a pregnant woman with hypothyroidism. Fertil Steril 2007; 88:705

41. Akbay E, Uzuncakmak C, Jdil N, Akcig Z, Ozl G, Yasar L. Recurrent Spontaneous ovarian hyperstimulation syndrome with hypothyroidism: A Case Report. Med J. of Bakirkoy. 2010; 6:42-5.

42. Sridev S, Barathan S. Case report on spontaneous ovarian hyperstimulation syndrome following natural conception associated with primary hypothyroidism. J Hum Reprod Sci 2013;5:158-61 .

43. Souza Lucas O, Areas Joao VI, Campos Maria C, Areas Isabela I, Resende Bruna AM, Spontaneous ovarian hyperstimulation syndrome in a pregnant woman with hypothyroidism: a case report. Feril Steril Rep. December 2021;2 (4):2266-3341. Available on: http://doi.org/10.1016/j.xfre.2021.07.004.

44. Suzuki, S. 2004. Comparison between spontaneous ovarian hyperstimulation syndrome and hyperreactio luteinalis. Arch. Gynecol. Obstet. 269:227-9.

45. HAIMOV-KOCHMAN R. YANAI N, YAGEL S, AMSALEM H, LAVY Y, HURWITZ.
spontaneous ovarian hyperstimulation syndrome and hyperreactio luteinalis are entities in continuum. Ultrasound Obstet Gynecol 2004;24:675-78. http:// www.interscience.wiley.com.Doi:10.1002/uog.1759.

46. Oztekin O, Soylu F, Tatli O. Spontaneous ovarian hyperstimulation syndrome in a normal singleton pregnancy. Taiwanese J Obstet Gynecol. September 2006;45(3):272-5.

47. Demirel E, Turhan U, Ekmekci E, Subasioglu A, Kelekci S. Severe Spontaneous ovarian hyper stimulation syndrome with cervical insufficiency: A case report. JFIV Reprod Med Genet 2016,4:2. http://dx.doi.org/10.4172/2375-4508.1000181.

48. Juan Gui, Jie Zhang, Wang-Ming Xu, and Lei Ming. Spontaneous ovarian hyperstimulation syndrome: Report of two cases. World J Clin Cases. 2019 Dec 26; 7(24): 4384–4390
.Published online 2019 Dec 26. doi: 10.12998/wjcc.v7.i24.4384 .

49. Rastin Z, Ghomian N, Khadem- Rezaiyan M. Severe ovarian hyper stimulation syndrome in a spontaneous

pregnancy with normal singleton fetus: A Case Report, Iran J Nurs Midwifery Res 2019;24:310-12.

50. 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.

51. 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. n engl j med 349;8 www.nejm.org august 21, 2003.

52. Vasseur C, Rodien P, Beau I, Desroches A, Gerard C, et al. (2003) A Chorionic gonadotropin sensitive mutation in the follicle stimulating hormone receptor as a cause of a familial gestational spontaneous ovarian hyperstimulation syndrome. N. Engl J Med 349: 753-9.

53. De Leener A, Caltabiano, G., et al. 2008. Identification of the first germ line mutation in the extracellular domain of the follitropin receptor responsible for spontaneous ovarian hyperstimulation syndrome. Hum. Mutat. 29,91-98.

54. Cardoso CG, Graca LM, Dias T, Clode N, Soares L, Spontaneous ovarian hyperstimulation and primary hypothyroidism with a naturally conceived pregnancy. Obstet Gynecol 1999;93:809-11

55. 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.

56. Montanelli, L., Van Durme, J.J., Smits G. et al 2004. Modulation of ligand selectivity associated with activation of the transmembrane region of the human follitropin receptor. Mol. Endocrinol. 18, 2061-73.

57. Vassart G, Pardo L, Costagliola S. A molecular dissection of the glycoprotein hormone receptors. Trends Biochem Sci 2004;29:119-26.

58. Roperts JE, Spandorfer S, Fasouliotis SJ, Lin K, Rosenwaks Z (2005) Spontaneous ovarian hyperstimulation caused by a follicle-stimulating hormone secreting pituatory adenoma. Fertil Steril 83:208-10.

59. Yilmaz EP. Topdagi, Yapca OM, Topagi YE, Topagi SK, Kumptepe Y. Spontaneous ovarian hyperstimulation syndrome with FSH receptor gene mutation: two rare case reports. case reports in obstetrics and gynecology 2018. http//doi.org/10.1155/2018/9294650.

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