

Spontaneous Ovarian Hyperstimulation Syndrome with Unknown Etiology: Case Report

ETİYOLOJİSİ AÇIKLANAMAYAN SPONTAN OVARİAN HİPERSTİMULASYON SENDROMU

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Abstract

Ovarian Hyperstimulation Syndrome (OHSS) associated with a spontaneously conceived singleton pregnancy is rare. Many etiologic factors are detected in spontaneous OHSS. None of them was seen in this case.

In this case ultrasonography of a 23 year-old woman revealed 5 weeks gestational sac with normal appearing ovaries. 2 weeks later ultrasonography revealed a viable fetus of 7 weeks gestation and enlarged, polycystic ovaries with free fluid in the pelvis. Laboratory studies, thyroid function tests, colour doppler analysis were normal. At 17 weeks gestation, ultrasonography revealed normal ovaries. The pregnancy proceeded normally. The ultrasound of ovaries, ovarian and thyroid function were normal 2 months after delivery.

OHSS is related to ovulation induction but rarely it may be related to PCOS, high endogenous gonadotropin levels, hyperandrogenism, multiple gestation, molar pregnancy, hypothyroidism, mutations in the FSH receptor gene and sometimes without any identifiable cause. Spontaneous OHSS can be managed conservatively without complication.

Key Words: Ovarian hyperstimulation syndrome, pregnancy

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Özet

Spontan gebeliklerde Ovarian Hiperstimulasyon Sendromu (OHSS) nadiren gelişir. Spontan OHSS'ye neden olan pek çok etiyolojik faktör vardır. Bu vakada bunların hiçbirine rastlanmamıştır.

Bu vakada, 23 yaşındaki bir kadında yapılan ultrasonografide (USG) 5 haftalık gestasyonel kese ile normal görünümlü overler tespit edildi. İki hafta sonra tekrarlanan USG'de 7 haftalık FKH (+) fetus ile bilateral polikistik, büyümüş overler ve pelviste serbest sıvı görüldü. Laboratuvar testleri, tiroid fonksiyon testleri, renkli doppler USG normaldi. 17. haftada tekrarlanan USG'de overler normal görünümdeydi. Gebelik normal seyrinde devam etti. Doğumdan 2 ay sonra yapılan USG, over ve tiroid fonksiyonları normaldi.

OHSS, ovulasyon indüksiyonu sonrası gelişir. Nadiren polikistik over sendromu, yüksek endojen gonadotropin seviyesi, hiperandrojenizm, çoğul gebelik, molar gebelik, hipotiroidizm, FSH reseptör genindeki mutasyonlar buna neden olabilir. Bazen hiçbir neden tespit edilemeyebilir. Spontan OHSS, komplikasyon gelişmeden konservatif olarak tedavi edilebilir.

Anahtar Kelimeler: Ovarian hiperstimulasyon sendromu, gebelik

Ovarian Hyperstimulation Syndrome (OHSS) is an iatrogenic disease with an incompletely described physiology. It's almost exclusively associated with ovulation induction, with gonadotropins or occasionally clomiphene citrate. OHSS associated with a spontaneously conceived singleton pregnancy is rare.

Case Report

A 23 year-old woman, para 4-2-1-1, was admitted to the hospital for secondary amenorrhea. Her medical-obstetric history and a review of systems was unremarkable. She had always been healthy, with regular menstrual cycles; she had not been on oral contraceptives nor had taken any other medication. She had never taken drugs for ovulation induction. Transabdominal US revealed 5 weeks gestational sac with normal appearing ovaries. Two weeks later pelvic sonography revealed an intrauterine single viable fetus of 7 weeks gestation according to crown-rump length measurement. Both ovaries enlarged, polycystic and measured 10 x 11 cm and 10 x 9 cm respec-

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tively, each containing 7-8 enlarged follicles. A minimal amount of free fluid was observed in the pelvis. The liver and kidneys were normal. Colour-Doppler analysis of the ovarian vessels excluded the presence of pathological flow. The diagnosis of grade 3 moderate OHSS was made, according to Golan's classification.¹

Patient had moderate pelvic pain and nausea. Laboratory study revealed: Hb; 13 gr/dl, Htc; 36, WBC; 13400, Na; 135 mEq/l, K; 5.2 mEq/l, BUN; 12 mg/dl, creatinine; 0.5 mg/dl, FBS; 65 mg/dl, AST; 44 U/l, ALT; 40 U/l, ALP; 117 U/l, total protein; 5.1 g/dl, albumin; 3 g/dl, total bilirubin; 0.5 mg/dl. PT, APTT, urine analysis and thyroid function tests were normal. Written informed consent was obtained from the subject. No treatment was given and patient called back two weeks later.

She came back 6 weeks later. The ultrasonography revealed the fetus of 13 weeks gestation with positive cardiac activity. The ovaries measured 8 x 9 and 7 x 8 cm respectively, each containing 2-4 enlarged (4 cm) follicles and no ascites was seen. The clinical conditions and the laboratory testing were stable during the following weeks. At 16 weeks the triple test was performed. HCG, oestradiol and α -fetoprotein values were normal, giving a risk factor of 1:1200 for Down syndrome.

At 17 weeks gestation, ultrasonography revealed normal sized ovaries. The fetus was compatible with 17 weeks of gestation and the placenta was grade 1-located in fundus.

The pregnancy proceeded normally and a healthy 3350 g male infant was born at 39 weeks of gestation by elective cesarean section. The ovaries had normal appearance during operation and at the ultrasound scanning 2 months after delivery. Ovarian and thyroid function were normal as well, as indicated by the plasma concentrations of follicle stimulating hormone, luteinizing hormone, prolactin, oestradiol, testosterone, dehydroepiandrosterone sulphate, androstenedione, free triiodothyronine, free thyroxine and thyroid stimulating hormone.

Discussion

In this report, a case of OHSS occurring spontaneously in association with a pregnancy of 7-week gestation was described. OHSS was developed in 2 weeks. Diagnosis further confirmed by complete resolution of the ovarian hyperstimulation, as demonstrated by clinical and ultrasonography and other laboratory data.

The OHSS is a serious complication of induction of ovulation with gonadotropins. It's rare in unstimulated cycles. Several mechanisms may be involved. These include an underlying polycystic ovary syndrome and high endogenous gonadotropin levels. Relatively high early follicular-stage estradiol levels, high androgen levels and dissynchrony in follicular recruitment and maturation are found in patients with polycystic ovary syndrome. It's possible that rare occurrence of a spontaneous LH surge and ovulation in an unstimulated cycle may, by a similar mechanism, lead to OHSS.² In this case, the patient did not show any signs of hyperandrogenism or of polycystic ovary syndrome, as confirmed by the blood and ultrasound examinations that were performed a few months after delivery. Also she had regular menstrual cycles before pregnancy.

Endogenous HCG secreted by the trophoblast 7-8 days after fertilization might represent an additional factor in sustaining and exacerbating ovarian hyperstimulation.³ Elevated concentrations of HCG and spontaneous OHSS have been described in twins⁴ as well as in molar pregnancies,⁵ but also in one case of normal singleton pregnancy.⁶ On the other hand, normal concentrations of HCG are reported in spontaneous OHSS.³ In our case HCG value was normal at 16 weeks. Therefore, HCG may not be the trigger in every instance of OHSS.

The association of spontaneous OHSS with hypothyroidism was described in two case reports.^{7,8} In women with hypothyroidism, the elevated concentrations of thyroid-stimulating hormone may mediate an ovarian hyperstimulation because of the presence of nuclear thyroid recep-

tors TR α and TR β in the granulosa cells. In this case the hormonal tests for thyroid function were normal during 1st trimester and 2 months after delivery.

Recently, spontaneous and recurrent occurrence of OHSS was shown in families which is caused by mutations affecting the follitropin receptor (FSHr). Mutations in the FSH receptor gene display an increased sensitivity to hCG and may be responsible for the development of OHSS. In the iatrogenic form, the follicular recruitment and enlargement occur during ovarian stimulation with exogenous FSH, while in the spontaneous form, the follicular recruitment occurs later through the stimulation of the FSH receptor by pregnancy-derived hCG. FSHr mutant shows an increase of its sensitivity to both hCG and TSH, together with an increase in basal activity.^{9,10} In this report, OHSS was not seen in previous pregnancies of patient. If there was a genetic component, it must be seen in all pregnancies. So receptor defect was not thought in this case.

The diagnoses of molar pregnancy and ovarian cancer were excluded; the former because the β -subunit HCG concentrations were low, the latter because the ultrasonographic examination revealed the classic "spokewheel" appearance that is characteristic of theco-luteal cysts, while colour-Doppler analysis of the ovarian vessels excluded the presence of pathological flow. Serum CA 125 measurements were not useful for the differential diagnosis since they were elevated, as expected in patients with gross ovarian enlargement.

Spontaneous OHSS is extremely rare. OHSS is almost always related to ovulation induction but rarely it may be related to PCOS, high endogenous gonadotropin levels, hyperandrogenism, multiple gestation, molar pregnancy, hypothyroidism,

mutations in the FSH receptor gene and sometimes without any identifiable cause. Etiology of OHSS is not completely identified yet. New studies are needed to clarify the causes of OHSS. Spontaneous OHSS can be managed conservatively without any complication.

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