doi: 10.5505/abantmedj.2020.68926

Abant Tıp Dergisi

Olgu Sunumu / Cilt 9 Sayı 1 Yıl 2020

Abant Medical Journal

Case Report / Volume 9 Issue 1 Year 2020

# Uzun Süreli Kombine Oral Kontraseptif Kullanımının Bırakılmasından Sonra Oluşan Spontan Bir Gebelikte Ovarian Hiperstimülasyon Sendromu: Bir Olgu Sunumu

## Ovarian Hyperstimulation Syndrome in A Spontaneous Pregnancy After Cessation of A Long-Term Combined Oral Contraceptive Use: A Case Report

Ayse Nur Aksoy[1], Ebru Bulut Erdem[2], Elcin Telli[3]

[1]Sağlık Bilimleri Üniversitesi, Erzurum Bölge Eğitim ve Araştırma Hastanesi, Kadın Hast. ve Doğum Bölümü, Erzurum, Türkiye
[2]Nenehatun Kadın Doğum Hastanesi, Kadın Hast. ve Doğum Bölümü, Erzurum, Türkiye
[3]Nenehatun Kadın Doğum Hastanesi, Jinekolojik Onkoloji Bölümü, Erzurum, Türkiye

**Öz**

Ovarian hiperstimülasyon sendromu (OHSS), ovulasyon indüksiyonunun veya kontrollü ovarian hiperstimülasyonun iatrojenik bir komplikasyonudur. Ovarian hiperstimülasyon sendromu, kontrollü ovarian hiperstimülasyon sikluslarında insan koryonik gonadotropin (hCG) uygulamasından dolayı sıklıkla meydana gelir. Ancak, normal spontan gebelik vakalarında OHSS nadir olarak bildirilmiştir. Bu yazıda, uzun süreli kombine oral kontraseptif kullanımının kesilmesinden sonra spontan gebe kalan, tekil gebeliği olan bir kadında, 10 hafta 5 günlük gebelik haftasında orta şiddette OHSS vakası bildirilmiştir. Uzun süreli oral kontraseptif kullanan hastalar erken tanı için OHSS semptomları hakkında bilgilendirilmelidir. Erken tanı ve uygun destek tedavisi, OHSS'nin yaşamı tehdit edici komplikasyonlarından kaçınmak için esastır.

**Anahtar Kelimeler:** ovarian hiperstimülasyon sendromu, kombine oral kontraseptif, gebelik

**Abstract**

Ovarian hyperstimulation syndrome (OHSS) is an iatrogenic complication of ovulation induction or controlled ovarian hyperstimulation. The OHSS frequently occurs due to the administration of human chorionic gonadotropin (hCG) in controlled ovarian hyperstimulation cycles. However, OHSS has been reported rarely in normal spontaneous pregnancy cases. In this paper, a case of mild OHSS at 10 weeks 5 days of gestation in a woman with singleton gestation, who conceived naturally after cessation of a long-term combined oral contraceptive use was reported. Patients using long-term oral contraceptive should be informed about the symptoms of OHSS for early diagnosis. Early diagnosis and appropriate supportive therapy are essential to avoid the potentially life-threatening complications of OHSS.

**Keywords:** ovarian hyperstimulation syndrome, combined oral contraceptive, pregnancy

## INTRODUCTION

Ovarian hyperstimulation syndrome (OHSS) is an iatrogenic complication of ovulation induction or controlled ovarian hyperstimulation (COH). Its clinical manifestations are cystic enlargement of the ovaries, abdominal pain, nausea, vomiting, ascites, tense distension, dyspnea, oliguria, electrolyte imbalance and hemoconcentration (1). There is a fluid shift from the intravascular to the third space due to increased capillary permeability and ovarian neoangiogenesis. The vasoactive substances secreted by ovaries under human chorionic gonadotropin (hCG) stimulation plays a major role in the increasing of capillary permeability. The OHSS frequently occurs due to the the administration of hCG in COH cycles (2,3). However, OHSS has been reported rarely in normal spontaneous pregnancy cases (4,5).

In this paper, we reported a case of mild spontaneous OHSS at 10 weeks 5 days of gestation in a woman with singleton gestation, who conceived naturally after cessation of a long-term combined oral contraceptive (OCP) use.

## CASE REPORT

Written informed consent was obtained from the patient for publication of this case report. A 31-year-old Turkish woman, gravida 2, para 1,

**İletişim Bilgisi / Correspondence**
Doç. Dr. Ayse Nur Aksoy, Sağlık Bilimleri Üniversitesi, Erzurum Bölge Eğitim ve Araştırma Hastanesi, Kadın Hast. ve Doğum Bölümü, Erzurum - Türkiye
**E-mail:** draysenuraksoy@hotmail.com
**Geliş tarihi / Received**: 20.10.2019 **Kabul tarihi / Accepted:** 27.12.2019 **Çıkar Çatışması / Conflict of Interest:** Yok / None

visited our hospital initially at the ten weeks of gestation for an antenatal check. Seven years ago, the patient delivered a healthy female baby at full term. She had been on cyclic birth control pills containing 30 microg ethinylestradiol and 3 mg drospirenone (Yasmin®, Schering AG, Berlin, Germany) for six years non-stop. She had no history of ovulation induction or any medication within the last 6 months except oral contraceptive. Se had stopped using oral contraceptives a month ago. She had no polycystic ovary syndrome and diabetes mellitus. The general appearance was good, she had mild abdominal distension and pain. Her blood pressure was 120/70 mmHg; pulse rate was 75 beats per min and respiration rate was 18/min. Ultrasonographic examination revealed an intrauterine pregnancy, with a fetal crown–rump length of 38.6 mm, which corresponded to the 10th week 5 days of gestation and normal heartbeat (Figure 1). Ultrasonography also showed bilateral multilocular cystic masses measuring 16.5 cm in size on the left and 16 cm on the right (Figure 2).

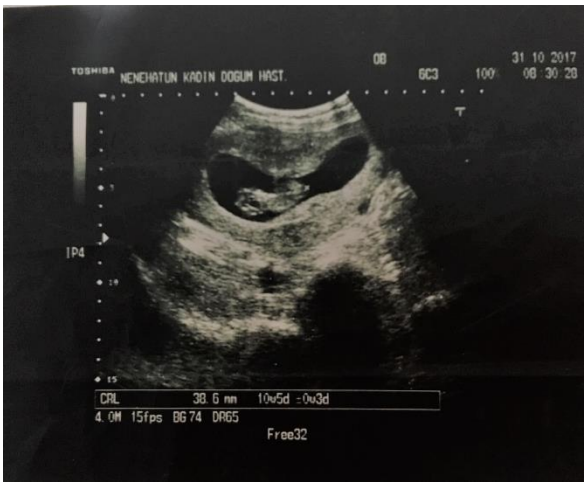


**Figure 1:** Intrauterine live fetus at 10 weeks 5 days of gestation


**Figure 2:** Ovarian enlargement with multiloculated cyst

She had a hemoglobin level of 11.9 g/dL, hematocrit was 37.1%, the white blood cell count was 12,700/mm3 and platelet count was 320,000/mm3. Estradiol level was 5,500 pg/mL. Other laboratory findings, including blood coagulation, liver function, renal function tests and blood electrolytes were normal. The diagnosis of mild spontaneous OHSS was considered. She was carefully monitored; body weight and abdominal circumference were measured every other day. Also, ultrasonography and laboratory tests including complete blood count, serum electrolytes and albumin concentrations were measured every other day. Ten days after admission, the laboratory findings remained stable and she was discharged.

During the following 8 weeks, laboratory findings remained within normal ranges and ultrasound examination revealed that the right adnexus had decreased to 4 cm in diameter and the left to 3 cm in diameter. The pregnancy progressed to 39 weeks of gestation. The patient had spontaneous onset labor and underwent an uncomplicated vaginal delivery of a healthy normal female baby of 3600 g was delivered.

## DISCUSSION

In this current case, we presented a case of mild spontaneous OHSS at 10 weeks 5 days of gestation in a woman after cessation of a long-

term combined OCP use.

The OHSS is characterized by cystic enlargement of the ovaries. It usually occurs due to the administration of human chorionic gonadotrophin (hCG). Although the pathophysiologic mechanism underlying OHSS has not to be known, it is thought that the degree of ovarian follicular response is responsible for the severity of this syndrome. Increased capillary permeability and ovarian neoangiogenesis induced by vascular endothelial growth factor and several pro-inflammatory cytokines are important in the pathophysiology of OHSS. The increase in capillary permeability leads to the fluid shift from the intravascular to the third space. Serum levels of estrogens produced by the developing follicles is used to detect the degree of ovarian hyperstimulation. Most of the cases with OHSS regresses spontaneously and pregnancy continues healthy in most cases. However, OHSS may be life-threatening due to the hypovolemia, haemorrhage from ovarian rupture, renal failure, acute respiratory distress syndrome and thromboembolic events. Outpatient management is usually applied for patients with mild or moderate. Hospitalization is required in women with critical OHSS and the multidisciplinary approach is essential for treatment. The main principles in the management of OHSS are careful monitoring of hemodynamic parameters, appropriate management of fluid balance, intravenous crystalloid and albumin infusion and prophylaxis of thrombosis (1-3).

There are two distinct patterns of OHSS: The early-onset form occurs 3–7 days after hCG trigger, and the late-onset form occurs 12–17 days after hCG. The occurrence of OHSS in an early-onset pattern is associated with exogenously administered hCG while the late pattern is related to the endogenous stimulation of hCG secretion from an implanted pregnancy. In both types of OHSS, hCG is thought to play a key role in the development of OHSS (6). The OHSS is rarely seen in spontaneous cycles (4,5). Spontaneous OHSS usually develops at 8–14 weeks of gestation, while iatrogenic OHSS generally reported to develop between 3 and 8 weeks of gestation. Underlying diseases such as polycystic ovary syndrome, multiple gestation, molar pregnancy, hypothyroidism, hyperandrogenism and mutations in the FSH receptor gene were thought to be the factors leading to the development of spontaneous OHSS (1-3). In this present case, the patient visited our hospital initially at the ten weeks of gestation for an antenatal check. So, we have got no information about the patient's findings and signs at the beginning of pregnancy. On the other hand, the patient had no underlying disease and she did not have a history of OHSS in her previous pregnancy. However, she had been on cyclic birth control pills containing 30 microg ethinylestradiol and 3 mg drospirenone for six years non-stop. As it known, oral contraceptives prevent ovulation by suppressing hypothalamic and pituitary secretion of hormones and they lead to thicken cervical mucus and prevent sperm penetration. Oral contraceptive pills (OCP) are widely used as adjunct treatment prior to ovarian stimulation during in vitro fertilization cycles. Oral contraceptive pretreatment helps to downregulate the patient’s hypothalamic pituitary axis and improves follicular synchrony (7). It was shown that OCP pretreatment increases the number of oocytes for retrieval and improves pregnancy rates in poor responders (8). Pan et al. (9) reported that the use of successive OCP (≥3 months) improves serum hormone levels, antral follicle counts and pregnancy rates in women with polycystic ovary syndrome undergoing IVF treatment compared with normal controls. Considering the results of these studies, it may be speculated that long-term OCP use may lead to the high follicular estradiol levels inhibiting follicle depletion.

To the best of our knowledge this is the first case of ovarian hyperstimulation syndrome in a spontaneous pregnancy after cessation long-

term combined oral contraceptive use. It should be considered that OHSS may ocur in patients using long-term OCP. So, these patients should be informed about the symptoms of OHSS for early diagnosis. Early diagnosis and appropriate supportive therapy is essential to avoid the potentially life-threatening complications of OHSS.

**Informed Consent:** Written consent was obtained from the participants.

**Conflict of Interest:** Authors declared no conflict of interest.

**Financial Disclosure:** Authors declared no financial support

## REFERENCES

1. Bhavsar PN, Padwal NJ, Bhide M, Ghagare SP, Joshi AR, Karnik ND. Life-threatening Medical Complications Due to Ovarian Hyperstimulation Syndrome: A Hidden Etiology. J Assoc Physicians India 2017; 65: 87-91.
2. Eskew AM, Omurtag KR. Ovarian hyperstimulation syndrome management strategies: where are we going? Minerva Endocrinol 2018; 43: 50-6.
3. Nelson SM. Prevention and management of ovarian hyperstimulation syndrome. Thromb Res 2017; 151: 61-4.
4. Cabar FR. Ovarian hyperstimulation syndrome in a spontaneous singleton pregnancy. Einstein (Sao Paulo) 2016; 14: 231-4.
5. Dey AK, Dubey A, Mittal K, Kale S. Spontaneous ovarian hyperstimulation syndrome understanding the dilemma. Gynecol Endocrinol 2015; 31: 587-9.
6. Ozay C, Emekci O, Okyay RE, Gülekli B. Ovarian Hyperstimulation Syndrome. Turkiye Klinikleri J Gynecol Obst-Special Topics. 2015; 8: 112-5.
7. Pinkas H, Sapir O, Avrech OM, Ben-Haroush A, Ashkenzi J, Fisch B, Farhi J. The effect of oral contraceptive pill for cycle scheduling prior to GnRH-antagonist protocol on IVF cycle parameters and pregnancy outcome. J Assist Reprod Genet 2008; 25: 29-33.
8. Kim CH, You RM, Kang HJ, Ahn JW, Jeon I, Lee JW, Kim SH, Chae HD, Kang BM. GnRH antagonist multiple dose protocol with oral contraceptive pill pretreatment in poor responders undergoing IVF/ICSI. Clin Exp Reprod Med 2011; 38: 228-33.
9. Pan JX, Liu Y, Ke ZH, Zhou CL, Meng Q, Ding GL, Xu GF, Sheng JZ, Huang HF. Successive and cyclic oral contraceptive pill pretreatment improves IVF/ICSI outcomes of PCOS patients and ameliorates hyperandrogenism and antral follicle excess. Gynecol Endocrinol 2015; 31: 332-26.