

Ovarian Hyperstimulation Syndrome in a Patient with One Ovary

TEK OVERİ OLAN BİR HASTADA OVARIAN HİPERSTİMÜLASYON SENDROMU

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Summary

Objective: To show that severe ovarian hyperstimulation syndrome can be seen in a patient with one ovary, despite to a low preovulatory estradiol level and a few follicle numbers.

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Case Report: A 23 – year old gravida 0, para 0 women, who had idiopathic hypothalamic primary amenorrhea admitted to our infertility clinic for to have a baby. Controlled ovarian hyperstimulation (COH) had commenced with FSH combined LH analogous. At the 13 th day of the protocol, serum estradiol level was 1090 ng/ml and sonographic examination showed 4 ovarian follicles in sizes of 21 mm, 17mm, 15mm, 14mm respectively. Preovulatory HCG (10000mIU) administration performed at the same day. The patient admitted to our out - patient clinic with the findings of severe ovarian hyperstimulation syndrome after the 14th day of the treatment protocol. After the infusions of balanced electrolyte solutions, albumin and also with the paracentesis done, the patient recovered.

Discussion: Severe OHSS can be seen in patients with one ovary despite to low preovulatory serum estradiol levels and a few numbers of preovulatory follicles. Attentive controlled ovarian hyperstimulation should be performed in these cases.

Key Words: Ovary, Ovarian hyperstimulation syndrome

T Klin J Gynecol Obst 2003, 13:155-157

Özet

Amaç; Tek overi olan bir hastada düşük preovulatuvar estradiol değeri ve az sayıda follikül sayısına rağmen şiddetli ovarian hipersitümüstasyon sendromunun gelişebileceğini göstermek.

Çalışmanın Yapıldığı Yer: Ege Üniversitesi Tıp Fakültesi Kadın Hastalıkları ve Doğum Ana Bilim Dalı.

Olgu Sunumu: Yirmi üç yaşında Gb1Po, bebek arzusu nedeniyle infertilite kliniğimize başvuran ve idiopatik hipogonadotropik hipogonadizmi olan hastaya, FSH ve LH analogu içeren bir rejim ile kontrollü ovarian hipersitümüstasyon başlandı. Uygulanan protokolün 13. gününde sonografik incelemede 21, 17, 15 ve 14 mm boyutlarında 4 adet ovarian follikül ve 1090 ng/ml serum östradiol değeri saptandı. Tedaviden 14 gün sonra hasta polikliniğimize şiddetli ovarian hipersitümüstasyon bulguları ile başvurdu. Dengeli elektrolit solüsyonları ve albumin infüzyonları ve parasetez uygulandıktan sonra hasta iyileşti.

Sonuç: Tek overi olan olgularda şiddetli OHSS düşük preovulatuvar serum östradiol değerleri ve az sayıda ovarian folliküle rağmen gelişebilmektedir. Bu olgularda kontrollü ovarian hipersitümüstasyon dikkatli bir şekilde uygulanmalıdır.

Anahtar Kelimeler: Over, Ovarian hipersitümüstasyon sendromu

T Klin Jinekoloj Obst 2003, 13:155-157

OHSS is characterized by cystic enlargement of the ovaries and various extragenital presentations, such as abdominal discomfort and gastrointestinal symptoms. Severe OHSS may include pleural and pericardial effusions, hypovolemia, and multiple organ failure. The incidence of ovarian hyperstimulation syndrome ranges from 3 to 8% for the mild forms and from 0.4 % to 4 % for the severe, potentially lethal, form (1). This syndrome occurs infrequently in natural, unstimulated cycles (2), but more frequently during or after controlled ovarian hyperstimulation (COH) with clomiphene citrate or highly purified gonadotropins (3).

The pathophysiology of this syndrome is not clear, but may be linked to inflammatory processes. Several recent reports suggest a pathophysiologic increase in serum

levels of inflammatory mediators such as vascular endothelial growth factor (4), various cytokines (5), prostaglandins (6), histamine and allergic individuals (7,8).

The identification of risk factors is crucial to prevention of OHSS. Multiple factors have been proposed to be related to an increased risk of OHSS. A number of limited and various control groups have been performed recently. In these studies, risk factors for the development of OHSS have been suggested, including high estradiol levels (COH>1700 pq/ml, IVF>4000 pq/ml), certain type of stimulation protocols (highly purified gonadotropins), multiple follicles at oocyte pick-up, a necklace ultrasound appearance of the ovaries before stimulation, low body weight, young age and support of the luteal phase with HCG (9,10). These risk factors especially serum estradiol

levels, are studied in patients with two ovaries and studies are lacking in patients with one ovary.

In this case we represent severe OHSS in a patient with hypothalamic amenorrhea with one ovary, and also with a few number of follicles and low serum estradiol level in the day of HCG administration. We sought to emphasize that severe OHSS can be seen in patients with one ovary, even with low estradiol levels and follicle numbers. Also we conclude that hypothalamic amenorrhea is a risk factor for the development of OHSS in patients with one ovary.

Case

A 23 – year old, gravida 0, para 0 women who had primary amenorrhea and married for two years had admitted to our infertility clinic for having a baby. She had idiopathic hypothalamic primary amenorrhea and had been using cyclic estrogen and progestin preparation for 8 years. She had left oophorectomy in our clinic for mature cystic teratoma two years ago.

The initial work up done for both of the partners at our infertility clinic revealed a normal spermiogram and a normal histerosalphingography. Basal serum FSH, LH, Estradiol, Prolactin levels of the patient were 0.1 < mIU/ml, 0.1 < mIU/ml, 20 < pq/ml and 20 ng/ml respectively which showed hypogonadotropic levels as mentioned above. Sonographic examination showed a normal uterus and a normal right ovary with absent left ovary.

Controlled ovarian hyperstimulation (COH), had commenced with FSH combined LH analogous. But she did not have sufficient follicular growth in this first protocol. Two months after the first COH, we had started the second stimulation protocol again with FSH combined LH analogous. We commenced the protocol with 75 IU in 2 x 2 doses / daily for 12 days. The gonadotropin dose is increased to 2 x 3 / daily, in the 8 th day of the protocol. Serum estradiol levels, sonographic diameter of the follicles and doses of the gonadotropin are shown in Table 1.

Serum estradiol levels were measured every 1-3 days during COH, and at least one transvaginal sonographic examination of the right ovary was performed during each week of COH to estimate follicular growth. At the 13 th day of the protocol, serum estradiol level was 1090 ng/ml and sonographic examination showed 4 follicles in sizes of 21 mm, 17mm, 14mm, 15mm respectively. Preovulatory HCG (10000mIU) administration performed at the 13 th day of the protocol. Ovulation of the largest follicle was confirmed sonographically 36 hours after the HCG administration and normal coitus scheme advised to the patient.

The patient admitted to our out - patient clinic complaining of abdominal bloating, shortness of breath and weariness fourteen days after the COH. Laboratory exami-

Table 1. Stimulation protocol with serum estradiol levels and follicle sizes

Menstruel Day	Stimulation Day	Estradiol Levels (pg/ml)	Follicule size and number (mm)	FSH& LH dosage (75 mIU)
3	1	<20	-	2x2
7	5	<20	Small	2x2
10	8	<20	Small	2x3
12	10	91	12, 8, 7, 6	2x3
14	12	640	17, 16 13, 14	2x3
15	13	1090	21, 17 14, 15	HCG 10.000 mIU

nation of the patient showed concordant findings with hemoconcentration in the serum. Serum β -HCG concentration was 139 mIU. Pelvic sonographic examination showed right ovary in size of 53x62 mm, which contained of six large cysts. The largest cyst was in size of 23x22 mm. Sonographic examination also showed severe pelvic and abdominal ascites.

She had been hospitalized for the treatment of severe OHSS. After the infusions of balanced electrolyte solutions, albumin and also with the paracentesis done, the patient recovered. Serum β -HCG concentrations showed a normal doubling time concordant with an intrauterin pregnancy. Luteal phase support was given with natural – progestin containing drug. At follow-up sonographic examination showed a viable intrauterin pregnancy. She had been discharged from the hospital without any complication.

Discussion

The cause of OHSS remains unclear. OHSS occurs after administration of menotropins and HCG and is associated with elevated serum levels of estradiol and with an increased number of preovulatory follicles (11), particularly those 15 mm diameter (10). Especially previous studies noted high serum preovulatory estradiol levels and these studies stated the critical preovulatory serum estradiol levels (COH>1700 pq/ml, IVF>4000 pq/ml) in patients whom OHSS developed (9,10). On the contrary, serum preovulatory estradiol level was low in the patient we have discussed.

Women with polycystic ovarian disease (group II) who develop many small follicles during ovulation induction are reported to be at increased risk for OHSS (12). After ovarian stimulation, the cumulative contribution of estrogens from multiple small follicles is presumed to be a causative factor in OHSS (12). Tulandi et al (13) however, did not find an increased risk in group II patients, moreover

reported a higher incidence in hypogonadotropic patients with amenorrhea. Because higher doses are needed for COH in hypogonadotropic patients, OHSS can be seen if estradiol levels are not strictly measured in these patients. Our patient was also hypogonadotropic.

Also there is an increased risk for the development of OHSS in younger age patients because of their increased sensitivity to ovulation induction (8,10). A plausible explanation for this age factor is that the ovaries in younger women are more responsive to gonadotropins because they have a higher density of gonadotropin receptors or a large number of follicles that are able to respond to gonadotropins. Our patient was also young.

Navot et al. (10) showed that low body weight is more common in patients with OHSS. In contrast, other investigators (8,14) were unable to find any difference in body mass index and weight and that assumption agrees well with the case we have discussed. The patient was not lean in our case.

A relevant marker for OHSS risk seems to be a large number of follicles present in the ovaries in the day of HCG administration. The classification of follicle size varies between studies (10,11). Blankstein et al (11) found that in patients with mild OHSS, 69 of the preovulatory follicles measured 9 - 15 mm, whereas in patients with moderate to severe OHSS, 95 % of the preovulatory follicles were < 16 mm, and most were 9 mm. In the study by Navot et al. (10), the ovaries of patients with OHSS contained increase number of follicles measuring 12 – 14 mm and > 18mm. Enskog et al. (8) emphasized that it may be useful to monitor both the total number of follicles and the number of large (>15 mm) follicles, in their study. The patient we had discussed, had four large preovulatory follicles in sizes of 21 mm, 17mm, 14mm, 15mm respectively and in accordance with Navot et al. (10) we noted that these follicle sizes were a risk factor for the development of OHSS. But the number of follicles in our case was less than the number of follicles in patients who had OHSS in previous studies (10,11).

The studies we have discussed above did not mention critical serum preovulatory estradiol levels, follicle sizes and numbers for the development of OHSS in patients with one ovary. Also we did not find relevant studies in the literature.

In conclusion, this case emphasize that OHSS can be seen in patients with one ovary, even within low preovulatory serum estradiol levels and a few numbers of preovulatory follicles.

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Geliş Tarihi: 20.03.2002

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