Rare manifestations of the ovarian hyperstimulation syndrome: a report of two cases

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Summary

The increasing practice of ovulation induction has made ovarian hyperstimulation syndrome (OHSS) a frequent clinical problem which can also become life-threatening. Two unusual cases of OHSS are described. The first patient presented with a unilateral pleural effusion. The second patient developed severe OHSS after a low-dose protocol with highly purified follicle stimulating hormone (FSH HP) and in the absence of risk factors.

Key words: OHSS; Pleural effusion; Highly purified follicle stimulating hormone; Low dose protocol.

Introduction

Ovarian hyperstimulation syndrome (OHSS) has become a more frequent problem with the increased use of exogenous gonadotropins for conventional ovulation induction (COI) or controlled ovarian hyperstimulation and assisted reproduction (COH/AR). OHSS occurs in mild, moderate and severe forms [1]. The incidence of OHSS after exogenous gonadotropin therapies is 0.5% to 10% [2, 3]. The severe form accounts for up to 2% of cases, is potentially life-threatening and requires hospitalisation [3].

We describe two patients without risk factors for OHSS who developed unusual and severe forms of the condition after assisted-reproduction techniques. The first patient presented with a massive unilateral pleural effusion. The second patient developed a severe OHSS after ovarian stimulation with highly purified follicle-stimulating hormone (FSH HP) in a low-dose protocol.

Patient 1

A 29-year-old woman presented with progressive dyspnea, bilateral chest pain and nausea 12 days after oocyte retrieval following COH elsewhere for male factor infertility. Down regulation was followed by HMG stimulation (Pergonal, Serono, Vienna) and hCG (Pregnyl, Organon, OSS, Vienna) application. Fertilisation occurred after intracytoplasmatic sperm injection (ICSI). Menarche took place at the age of 15 years and menstruation was normal. Hormonal state parameters before COH/AR were normal and there were no signs of PCOD. Physical examination showed a 155 cm, 63 kg (+ 8 kg since hCG application) patient with dullness on the percussion over the left hemithorax with ipsilateral decreased respiratory sounds. On palpation, the abdomen was soft, nontender and nondistended. Chest radiography showed a massive left-sided pleural effusion (Fig. 1). Vaginal ultrasound on the day of admission showed enlarged ovaries with the largest diameter 90 mm but no ascites (Fig. 2). Laboratory studies showed leucocytosis (35.700 / mm^3), haemoconcentration (haematocrit 49%), and hypoalbuminaemia (3.4 g/dL). The estradiol level was 1510 pg/mL and ß-hCG was positive in the urine.

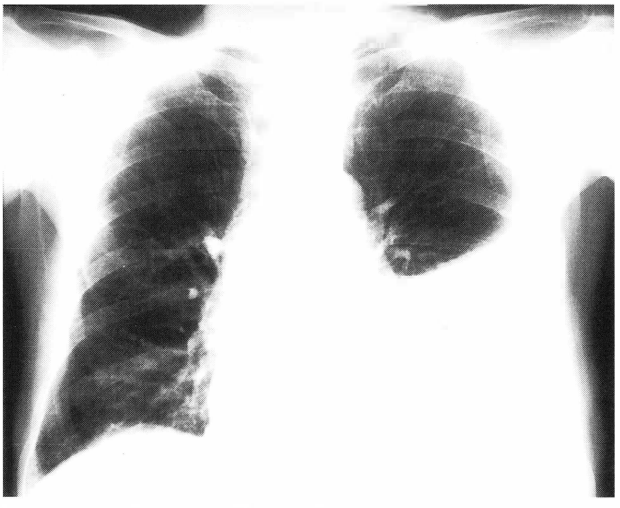

Figure 1. — Patient 1. Chest radiograph in patient 1 on the day of admission. There is an unilateral pleural effusion.

Supportive treatment failed to improve the condition. Severe respiratory insufficiency developed on the third day of hospitalisation and on day 4 the patient developed bilateral pleural effusions and minimal ascites even though leucocytosis declined to 12.000 / mm^3 and the haematocrit to 38%. The pleural effusions were treated with four thoracocenteses over 3 days, removing a total of 4000 mL. Dyspnea resolved with thoracocenteses. By day 12 all laboratory parameters were normal and the patient was discharged feeling well on day 13. The further course of the twin gestation was uneventful.

Patient 2

A 30-year-old woman underwent IVF at our unit for primary infertility and dysmenorrhea. Menarche took place at the age of

Received July 3, 1997
revised manuscript accepted for publication August 10, 1997

14. Except for dysmenorrhea no other menstrual anomalies were present.

Physical examination showed a healthy woman: height 1.65 m., weight 62 kg. Hormonal state parameters, were within normal range. Gyneacological examination, sonography and hormonal state parameters showed no pathological findings. Semen analyses were normal. Endoscopic examination showed a severe primary tubal sterility. The patient was treated with a COH/AR long protocol. Down regulation with goserelin (Zoladex Depot 3.6 mg Implantat., Zeneca, Vienna) was followed by ovarian hyperstimulation with highly purified FSH (Fertinorm HP 75, Serono, Vienna). On the day of hCG administration (10.000 IU = 2 amp., Pregnyl, Organon, Vienna) 8 of 22 detected follicles were >12 mm in diameter and the estradiol level was as low as 694 pg/mL. All detected follicles were aspirated transvaginally and four embryos were transferred. HCG (2500 IU, with intervals of three days) and progesterone (600 mg/d intravaginally; Utrogestan©, 3x2 tabl, 100 mg; Laboratories Besins - Iscovesco, Paris) were applied in the corpus luteum phase. Six days after oocyte retrieval the patient developed abdominal complaints and dyspnea. Physical examination was normal except for a respiratory rate of 25/min. The abdomen was soft with some distention and signs of ascites. Sonography showed the ovaries - reaching up to the umblicus and ascites (Fig. 3). The estradiol level was as low as 314 pg/mL. Haemoconcentration (47%), leucocytosis (15.200/mm^3), and hypoalbuminemia (3.2 g/dL) were present. ß-hCG became positive on day 4 of hospitalisation.

The patient was hospitalised for 19 days and treated with supportive measures. The further course of the pregnancy was complicated by intrauterine growth retardation. A 976-g infant was delivered by ceasarean section at 32 weeks' gestation.

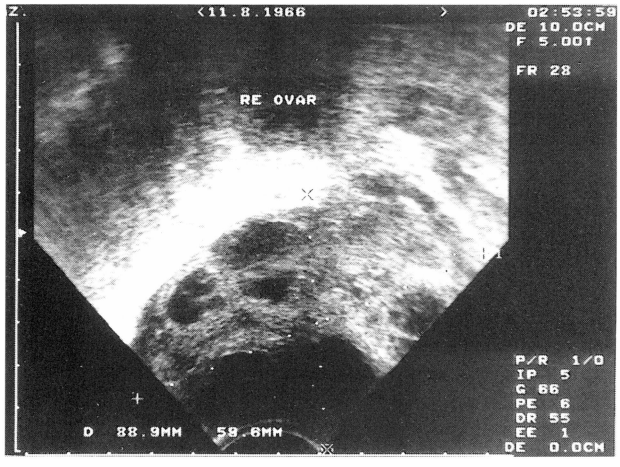

Figure 2. — Patient 1. Vaginal sonogram showing a cystic left ovary but no free fluid.

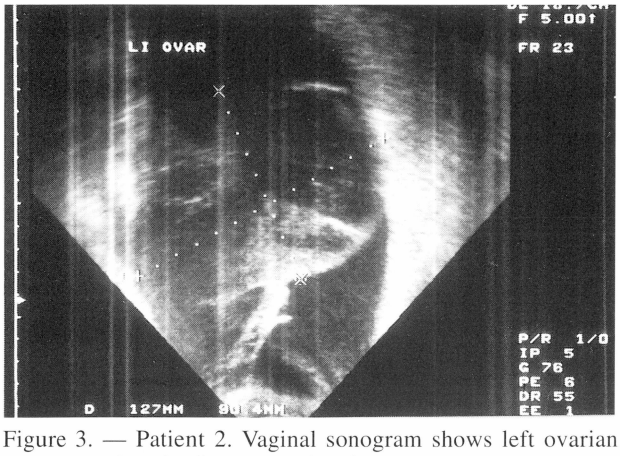

Figure 3. — Patient 2. Vaginal sonogram shows left ovarian cysts up to 6 cm in diameter and ascites.

Discussion

The pathophysiology of OHSS involves increased vascular permeability leading to extravascular exudates combined with intravascular volume depletion and haemoconcentration [4, 5]. Plasma renin-angiotensin [6], interleukin II [7, 8], prostograndins, histamine cytokines and vascular endothelial growth factor [9] are possible mediators.

The patients presented here are noteworthy because of their atypical presentation and because they did not have clinical or laboratory risk factors for OHSS. The second patient was puzzling because the serum estradiol level was considerably lower than expected after gonadotropin therapy (694 pg/ml at the time of hCG application). Others have reported that the level of estradiol in serum may be normal before manifestation of OHSS [7, 10]. Using hCG to trigger ovulation is a risk factor for OHSS [3, 7]. In both our patients intrinsic hCG secretion through gestation may have triggered or aggravated OHSS.

hCG can be withheld in patients considered at high risk of OHSS. Prolonged coasting [11], lower hCG dose [2], hCG substitutes like gonadotrophin releasing hormone agonist (GnRH-a) [12, 13], use of recombinant FSH [14] and follicular aspiration followed by cryopreservation [2] and transfer of the embryos during a natural cycle are current alternative methods. Low-dose FSH stimulation may lower the risk of OHSS and multiple pregnancies while maintaining a satisfactory pregnancy rate [15, 16] but did not prevent OHSS in our second patient.

Thoracic manifestations indicate a severe OHSS and are usually accompanied by other signs of the syndrome such as enlarged ovaries, ascites, oliguria, and haemoconcentration. So far there are only a few case reports presenting isolated hydrothorax [4-6] as a clinical manifestation of OHSS as in our first patient. However in our case main laboratory changes were present. The etiology of an isolated hydrothorax in OHSS remains unclear. Our patient did go on to develop bilateral pleural effusions and minimal ascites under supportive therapy, even as laboratory parameters improved.

Thoracocentesis is rarely necessary to relieve respiratory distress due to pleural effusion after exogenous gonadotropin therapy [21]. Our patient required multiple thoracocenteses whereas no paracentesis was necessary.

In summary, early recognition of clinical or laboratory risk factors and low-dose stimulation protocols do not offer absolute protection against OHSS. Furthermore, clinicians must be aware of the fact that the OHSS can present with unusual clinical manifestations, such as only unilateral pleural effusion.

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