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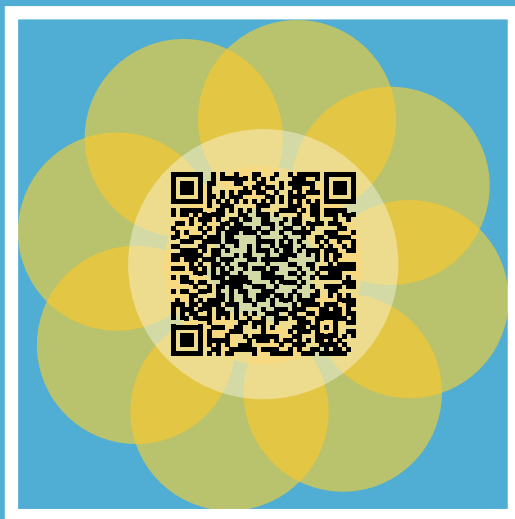
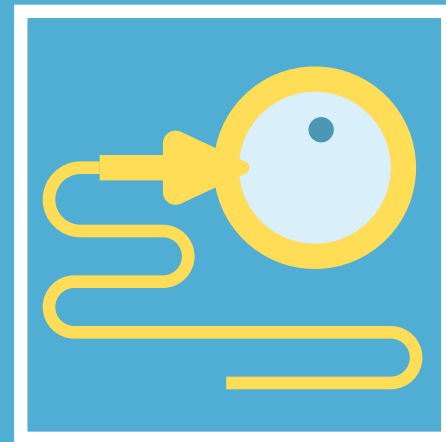
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## BACK TO THE FUTURE

# Differential Diagnosis of a Severe Late Onset Ovarian Hyperstimulation Syndrome Associated with Prolonged Ascites Production – a Case Report

E. Ujvari<sup>1</sup>, F. Krizsa<sup>2</sup>, A. Bernard<sup>2</sup>, S. Varbiro<sup>1</sup>, F. Paulin<sup>1</sup>

**Capsule:** A case of severe late onset ovarian hyperstimulation syndrome (OHSS) with prolonged ascites production. Difficulties of differential diagnosis and management. **Objective:** This report describes a case of extremely prolonged, severe ovarian hyperstimulation syndrome. **Results:** 17 litres of ascites have been removed from the abdominal cavity by repeated paracenteses until the 25<sup>th</sup> week of pregnancy, which progressed after the complete resolution of symptoms to the 34<sup>th</sup> week, when cesarean section was done. **Conclusion:** Severe ovarian hyperstimulation syndrome can occasionally follow an unusually prolonged course. Chronic formation of abundant ascites, the presence of ovarian enlargement and elevated levels of certain tumour markers might raise the probability of ovarian cancer. Adequate differential diagnosis and management resulted in delivery of a healthy newborn. *J Reprodukciomsmed Endokrinol* 2005; 2 (4): 259–61.

**Key words:** ovarian hyperstimulation syndrome, ascites, tumour marker

Prolonged occurrence of abundant ascites formation and elevated CA 125 level were observed in a *gravida* following *in vitro* fertilisation and embryo transfer (IVF-ET). Although clinical manifestations were suggestive of ovarian hyperstimulation, other diagnostic options to be ruled out included also ovarian cancer.

## Case Report

The history of a 33-years-old *gravida* comprises twin pregnancy following IVF-ET indicated by bilateral tubal occlusion and *uterus duplex*, resulted in delivery of healthy female twins by cesarean section. Before the current pregnancy also ovarian stimulation was performed according to the “flare-up” protocol. Three days after the puncture, three pre-embryos were transferred into the right uterine cavity. Human chorionic gonadotropin (hCG) 5000 IU was administered on the day of embryo transfer, then three times 2500 IU doses were given at 48 hours intervals, simultaneously with intravaginal micronised progesterone replacement (3 × 200 mg/day). Ultrasound performed in the 7<sup>th</sup> week of pregnancy revealed one intact embryo and a moderate enlargement of the ovaries, however the volume of peritoneal fluid was not significant.

Increasing bloating, abdominal tenderness and nausea appeared at the 11<sup>th</sup> week of pregnancy. Ultrasound depicted a viable embryo with a size corresponding to gestational age, as well as ascites of substantial volume (approx. 1000 ml) in the abdominal cavity. The dimensions of the right ovary were 75 × 64 × 50 mm; it contained three luteal cysts of 30 mm in diameter. The left ovary was moderately enlarged. Subjective symptoms and ultrasound findings suggested “grade 5 – severe” ovarian hyperstimulation syndrome (OHSS) by Golan [1].

On admission, body weight of the *gravida* was 56 kg (54 kg before IVF) whereas her abdominal circumference

was 93 cm. Peripheral edema and dyspnoe were absent. Laboratory work-up detected elevated platelet count (513 G/l), CRP (88 mg/l) and alkaline phosphatase level (666 IU/l). WBC and lymphocyte/granulocyte rate were normal, as well as total protein, serum sodium and potassium levels. Laboratory testing of hemostasis revealed high D-dimer (8 µg/ml) and fibrinogen (7.5 g/l) levels.

Thrombosis prophylaxis and intravenous fluid replacement were initiated as standard therapy for OHSS [2], while continuing high-dose progesterone substitution. Because of elevated CRP level, antibiotic therapy (amoxicillin + clavulanic acid, 3 × 625 mg/day) was also started.

No acute deterioration in the general condition of the *gravida* occurred during the following days. Nevertheless, anaemia (Hct: 28–30 %; Hb: 90–100 g/l) and proteinuria (1 g/l) ensued. Presumably, pre-existent anaemia had been masked by haemoconcentration accompanying hyperstimulation and therefore, it was not detected by early laboratory testing. Subsequent fluid replacement, however, revealed this abnormality along with low serum protein levels (48–52 g/l). Accordingly, oral anti-anaemic agents and parenteral protein replacement (200 ml 25 % human albumin) were added to the regimen [2]. The monitoring of laboratory parameters demonstrated slow improvement (WBC, CRP, D-dimer and fibrinogen levels) over the 12<sup>th</sup> and 13<sup>th</sup> weeks of pregnancy. Notwithstanding, the volume of ascites was increasing steadily despite treatment and the progress of pregnancy – both of which should have resulted in improvement [2]. The size of the right ovary increased further (105 × 75 × 60 mm). Fluid retention escalated with a correspondingly large (2.5–3.0 kg/week) increase in body weight (to 67 kg on 15<sup>th</sup> week). Therefore, oral antihistamine (chloropyramine chlorate 3 × 25mg/day) and intravenous glyocorticoid (oradexone 10 mg/day) were added to the therapy from the 14<sup>th</sup> week in order to reduce capillary permeability. Nevertheless, beyond worsening of symptoms (nausea, vomiting, wasting of extremities and face), increased abdominal circumference (145 cm), extreme ascites and concomitant dyspnoe developed. At the end of the 15<sup>th</sup> week of pregnancy paracentesis of the abdomen resulted in 10 litres of yellow exudate of high (42 g/l) protein content; cytology and culturing were negative, nor acid-fast bacilli were found by Ziel-Neelsen staining of the cellblock. The cir-

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From the <sup>1</sup>Semmelweis University, Faculty of Medicine, 2<sup>nd</sup> Department of Gynecology and Obstetrics, and the <sup>2</sup>Kaáli Institute, Budapest, Hungary

**Correspondence:** Elemer Ujvari MD, Semmelweis University, Faculty of Medicine, 2<sup>nd</sup> Department of Gynecology and Obstetrics, Budapest, Hungary; e-mail: ujvari@ana2.sote.hu



culuation of the *gravida* remained stable during paracentesis.

Paracentesis reduced body weight to 57 kg, abdominal circumference to 102 cm, and eliminated subjective symptoms. Despite ongoing therapy, abdominal circumference increased again from the next week. Ultrasonography demonstrated re-accumulation of ascites along with moderate enlargement of the ovaries (Fig. 1). Abdominal MRI excluded hepatic involvement (Budd-Chiari syndrome, liver cirrhosis, and hepatic metastases) and portal flowmetry was normal. Testing for hepatitis A, B, C, E, and toxoplasma, rubella and cytomegalovirus were negative, as well as thrombophilia checkup. However, a substantial elevation of CA 125 (to 274 IU/ml by week 18 and to 346 IU/ml by week 23) was detected, whereas other tumour markers (such as CEA, CA 19-9) stayed in the normal range. Elevated CA 125 level, chronic ascites formation and low-impedance flow recorded on ovarian flowmetry however were suspicious for ovarian cancer (Fig. 2), but the negative cytology of peritoneal fluid contradicted this. Consequently, the abnormalities detailed above were interpreted as manifestations of unusually prolonged late onset ovarian hyperstimulation.

Subsequently, ascites production continued, although at a slower (1 kg/week) rate. The size of the ovaries decreased and this was accompanied by the resolution of laboratory abnormalities (CRP, D-dimer, serum protein levels). Anticoagulants and antibiotics were discontinued in the 20<sup>th</sup> week of pregnancy. Owing to the slow but consistent accumulation of peritoneal fluid and recurrence of subjective symptoms, paracentesis was repeated in week 25; 7 litres of yellow fluid were emptied, containing similar components as the ones mentioned above. CA 125 level of the ascites was 2627 IU/ml; however, no other tumour markers were detected.

Afterwards, follow-up ultrasound examinations failed to detect ascites formation, size of ovaries returned near to normal, fetal development was satisfactory, and laboratory parameters were normalised. All medication was ceased. Because of breech presentation and premature rupture of membranes in the 34<sup>th</sup> week, pregnancy was terminated by cesarean section. A healthy, female 2300 g neonate was delivered. In the abdominal cavity was not

detectable any alteration other than a negligible volume of ascites (100 ml). Intraoperative frozen-section and conventional histologic work-up of ovarian biopsy specimens were negative. Follow-up demonstrated decreasing (56 IU/ml) serum CA 125 level, without any postoperative complications.

## Discussion

Ovarian hyperstimulation syndrome (OHSS) is a severe and potentially life-threatening complication of controlled hyperstimulation [2, 3]. Likely predisposing factors include young age, low body mass index, polycystic ovaries, and rapid elevation of serum E2 levels during stimulation [3, 4]. Increase in endogenous hCG after implantation may initiate the "late onset" form of OHSS [5]. Enlargement of the ovaries, release of vasoactive substances and consequent enhancement of capillary permeability occurs [6]. The latter can induce accumulation of peritoneal, pleural, or pericardial fluid [2, 7]. Early subjective symptoms include bloating and abdominal tenderness, followed by nausea, vomiting, diarrhea and anorexia. Major ascites formation can result in weight gain with dyspnoe and oliguria. These changes may be accompanied by laboratory abnormalities, such as haemoconcentration, leukocytosis, hypoalbuminaemia, hyponatraemia and hyperkalaemia [8]. Hypercoagulability persisting in OHSS may cause thromboembolism [2, 3].

The case reported herein is remarkable for the unusually late manifestation of severe OHSS (in the 10<sup>th</sup> to 11<sup>th</sup> weeks of gestation), as well as for exceptionally prolonged and abundant ascites formation (until the 25<sup>th</sup> week); the latter is unprecedented in the literature. The extraordinary persistence of OHSS was a differential diagnostic problem. Unrelenting manifestations of ovarian hyperstimulation persisted despite standard therapy [1–3] and the progression of gestational age. Therefore, several diagnostic imaging studies and specific laboratory methods were made to exclude the possibility of other serious disorders. The only major abnormality was the extreme (ten-fold) elevation of the CA 125 level during the second trimester, raising the suspicion of ovarian cancer [9, 10]. According to the literature, OHSS is associated with marked elevation of the CA 125 level during the initial weeks of pregnancy and the magnitude of this elevation may be proportional to clinical severity [11]. However,

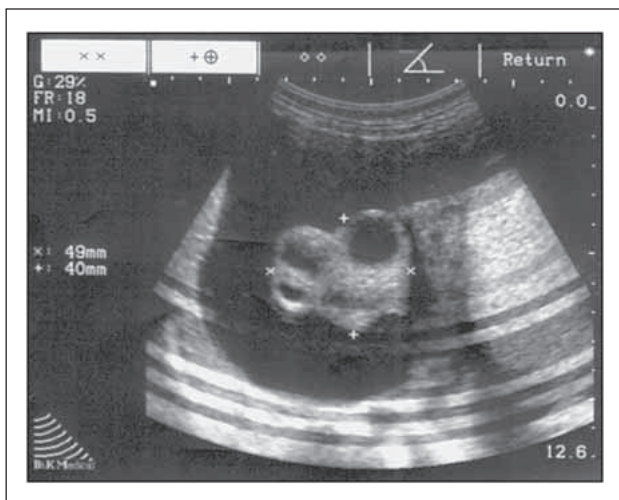


Figure 1. Enlarged ovary with cysts and surrounding ascites

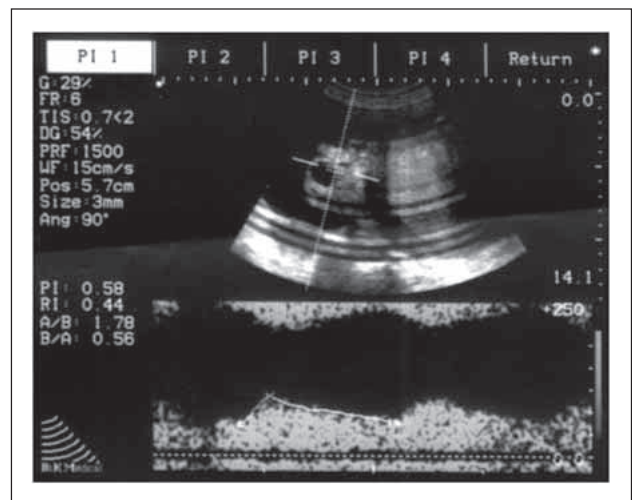


Figure 2. Low resistance blood flow in the enlarged, cystic ovary

we had not got data on the 2<sup>nd</sup> trimester of pregnancy. Although the substantial enlargement of cystic ovaries and low-impedance flow are known features of OHSS, their persistence may suggest also ovarian tumour [12]. Nevertheless, cytology of the peritoneal fluid obtained by abdominal paracentesis failed to identify tumour cells in our case and the levels of other tumour markers were normal. This was the most important fact, why the pregnancy was not terminated in the 15<sup>th</sup> week, and the patient also avoided from operative hystology. Therefore, the high CA 125 level observed during the second trimester of pregnancy was regarded as a hitherto unpublished component of the ovarian hyperstimulation syndrome. Seemingly, this is confirmed by the exploration of the peritoneal cavity upon cesarean section: neither intra-abdominal lesions, nor significant ascites was found. Inspection of the ovaries did not suggested malignancy; histologic samples obtained from the ovaries were negative.

### Conclusion

As evidenced by the case described herein, severe OHSS can follow an unusually prolonged course and may be associated with ascites formation alone, i.e. without hydrothorax or the accumulation of pericardial fluid. Extreme elevation of CA 125 level is a potential feature of OHSS in the 2<sup>nd</sup> trimester; however, its presence should prompt for excluding possibility of ovarian cancer. Importantly, OHSS is not associated with elevation of CEA and CA 19-9 tumour markers during the 2<sup>nd</sup> trimester.

Our case suggests, that it is crucial to distinguish between the two severe disorders because of the different management: if the prolonged symptoms are caused by ovarian cancer the termination of the pregnancy and elimination of tumour is necessary as soon as possible. In case of

hyperstimulation syndrome appropriate management is urgent for stabilising the patient's condition while preserving the life of the foetus.

### References:

1. Golan A, Ron-el R, Herman A, Soffer Y, Weinraub Z, Caspi E. Ovarian hyperstimulation syndrome: an update review. *Obstet Gynecol Surv* 1989; 44: 430–40.
2. Whelan JG, Vlahos NF. The ovarian hyperstimulation syndrome. *Fertil Steril* 2000; 73: 883–96.
3. ASRM. Ovarian hyperstimulation syndrome. *Fertil Steril* 2004; 82: S81–S86.
4. Orvieto R. Can we eliminate ovarian hyperstimulation syndrome? *Hum Reprod* 2005; 20: 320–2.
5. Lyons CA, Wheeler CA, Frishman GN, Hackett RJ, Seifer DB, Haning RV. Early and late presentation of the ovarian hyperstimulation syndrome: two distinct entities with different risk factors. *Hum Reprod* 1994; 9: 792–9.
6. Levin ER, Rosen GF, Cassidenti DL, Yee B, Meldrum D, Wisot A. Role of vascular endothelial cell growth factor in ovarian hyperstimulation syndrome. *J Clin Invest* 1998; 102: 1978–85.
7. Murray A, Rombauts L. Unilateral pleural effusion as the main presentation of "early onset" severe ovarian hyperstimulation syndrome. *Fertil Steril* 2004; 81: 1127–9.
8. Enskog A, Henriksson M, Unander M, Nilsson L, Brannstrom M. Prospective study of the clinical and laboratory parameters of patients in whom ovarian hyperstimulation syndrome developed during controlled ovarian hyperstimulation for in vitro fertilization. *Fertil Steril* 1999; 71: 808–14.
9. Bischof P. What do we know about the origin of CA 125? *Eur J Obstet Gynecol Reprod Biol* 1993; 49: 93–8.
10. Bast RC, Klug TL, Schaetzl E, Lavin P, Niloff JM, Greber TF, Zurawski VR, Knapp RC. Monitoring human ovarian carcinoma with a combination of CA 125, CA 19-9 and carcinoembryonic antigen. *Am J Obstet Gynecol* 1984; 149: 553.
11. Jager W, Diedrich K, Wildt L. Elevated levels of CA-125 in serum of patients suffering from ovarian hyperstimulation syndrome. *Fertil Steril* 1987; 48: 675–8.
12. Ditkoff EC, Tucker T, Levine RU, Lindheim SR, Sauer MV, Longacre T. Bilateral serous cystadenofibromas clinically simulating hyperreactio luteinalis following controlled ovarian hyperstimulation and in vitro fertilization. *J Assist Reprod Genet* 1997; 14: 230–3.

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