

General Section

Mild ovarian hyperstimulation syndrome coexisting with ectopic pregnancy after in vitro fertilization

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Summary

Ovarian hyperstimulation syndrome (OHSS) is an entity arising in women undergoing assisted reproductive techniques (ART). The simultaneous presence of two different clinical complications such as OHSS and ectopic pregnancy (EP) is not frequent. The diagnosis of an extrauterine pregnancy can be obscured by the stimulated ovaries and ascites, and actually be missed, especially in women with increased body mass index. We report a case of a woman who presented with mild OHSS after in vitro fertilization (IVF), (intracytoplasmic sperm injection (ICSI) and embryo transfer). The ectopic pregnancy was ascertained soon after by transvaginal ultrasound (TVS) and right salpingectomy was performed.

Key words: Mild OHSS; Ectopic pregnancy; Diagnosis.

Introduction

Ectopic pregnancy (EP) is a major health problem for women of reproductive age, especially in developed countries where the incidence of EP has increased six-fold the last 20 years [1]. The main cause of EP is considered to be endothelial damage of the tubes and subsequent dysfunction secondary to salpingitis.

In vitro fertilization (IVF) is an elective procedure and clinical problems arising from this treatment are always iatrogenic. Four major complications are reported: ovarian hyperstimulation syndrome, adnexal torsion, pelvic inflammatory disease and ectopic pregnancy [2].

Ovarian stimulation and in general the use of assisted reproductive techniques (ART) is associated with increased risk of EP with a frequency of 2.1 up to 11% [3,4], even in the absence of predisposing factors [5]. The uncommon incidence of the simultaneous presence of two different complications is reported.

Case Report

A 37-year-old woman presented at the Gynecology Outpatients Department with lower abdominal pain, discomfort and vaginal bleeding after IVF treatment (ICSI and embryo transfer). An abdominal ultrasound scan revealed bulky uterus, thickened endometrium, enlarged ovaries with multiple cysts, and fluid in the pouch of Douglas. A pregnancy test was positive and blood tests revealed elevated b-HCG, high levels of estradiol and mild electrolytic changes. Initial diagnosis was mild ovarian hyperstimulation syndrome (OHSS). However, a transvaginal ultrasound scan performed by a specialist revealed an unruptured right tubal pregnancy coexisting with the OHSS. Surgical treatment was decided and right salpingectomy by laparotomy was performed. The patient was closely followed-up with repeated scans and blood tests. The size of the ovaries and the level of b-HCG decreased gradually.

Discussion

All women who undergo ovarian stimulation during IVF, experience enlargement of their ovaries and a complex change in their hormone balance. This can be quite unpleasant with abdominal bloating and pelvic discomfort. It is expected that approximately 1% of the stimulated women will present with severe symptoms [6, 7]. The problem, labelled "ovarian hyperstimulation syndrome", is the most frequent complication of ovarian stimulation and usually presents a couple of days after embryo transfer. In fact, in IVF treatment the development of mild ovarian stimulation allows the recruitment of mature follicles.

The risk factors that independently increase the risk of developing OHSS are young age, low body weight, polycystic ovary syndrome (PCOS), higher doses of exogenous gonadotrophins, high absolute or rapidly rising serum estradiol levels and previous episodes of OHSS. Risk for developing OHSS also rises with the number of developing ovarian follicles and the number of oocytes retrieved in ART cycles, or when higher or repeated doses of exogenous human chorionic gonadotrophin (hCG) are administered in superovulation and ART cycles (for ovulation induction and luteal phase support). However, OHSS does not occur if the final hCG injection is not given. Risk decreases when exogenous progesterone, rather than hCG, is used to support the luteal phase, while pregnancy increases the likelihood, duration, and severity of OHSS symptoms [2].

OHSS is traditionally classified as mild, moderate, or severe, depending on the severity of electrolytic changes and the clinical features [6]. The pathogenesis of the syndrome still remains an enigma, but it seems that the activation of the renin-angiotensin-aldosterone system has a major role in the development of OHSS [2]. Essentially, fluid from the blood stream leaks into the abdominal cavity causing it to swell noticeably and leaving the blood more concentrated and more viscous. Mild mani-

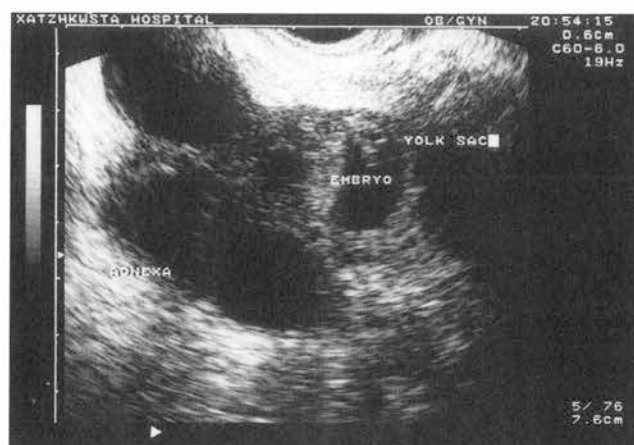


Fig. 1

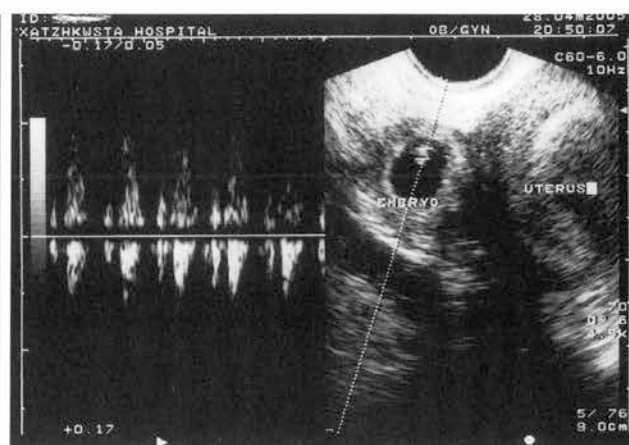


Fig. 2

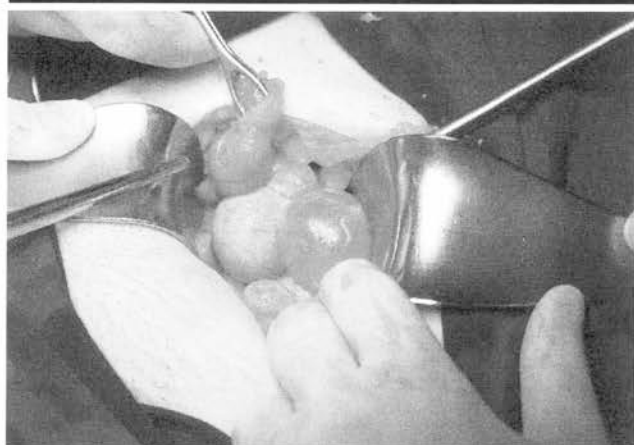


Fig. 3

Figure 1. — Transvaginal ultrasound. Common sonographic feature of an enlarged stimulated ovary with hemorrhagic lutein cysts or corpora lutea. Beside the right ovary the ectopic embryo can be seen.

Figure 2. — The empty uterine cavity and the ectopic gestation at the right side with positive embryonic heart rate.

Figure 3. — Macroscopic appearance

festations of OHSS are relatively common and include transient lower abdominal discomfort, mild nausea, vomiting, diarrhea and abdominal distention (observed in up to a third of superovulation cycles). Onset of symptoms typically occurs soon after ovulation (in superovulation cycles) or after oocyte retrieval in ART cycles, but it may be delayed. Progression of illness is recognized when symptoms persist, worsen, or include ascites that may be demonstrated by increasing abdominal girth or by ultrasound. Serious illness exists when pain is accompanied by rapid weight gain, tense ascites, hemodynamic instability (orthostatic hypotension, tachycardia), respiratory difficulty (tachypnea), progressive oliguria and laboratory abnormalities [8].

Cases of OHSS combined with ectopic, heterotopic, primary ovarian and primary abdominal pregnancy have been reported [9-12]. Actually, the first pregnancy obtained after IVF was ectopic [13]. During the embryo transfer procedure, the embryos could be flushed into the fallopian tubes. When the salpinx is normal the embryo mimicking the fertilized ovum returns to the uterine cavity, but when tubal dysfunction exists, the risk of ectopic pregnancy is higher. Due to this potentially serious problem some authors, [14, 15] have advised bilateral occlusion of the utero-tubal junction but clarified that removal is not necessary. Nevertheless, Karande *et al.* reported two interstitial pregnancies after IVF in patients who underwent salpingectomy [16].

The embryo transfer technique is by itself a factor for EP [2]. Knutzen *et al.* [17] suggested transfer of embryos in a small amount of culture fluid in an attempt to prevent reflux, while Yovich *et al.* inserted the catheter 55 mm only achieving a standard mid-cavity position [18]. In general the risk of EP is increased by 3.88 after a difficult transfer and by 5.41 when there is a history of previous ectopic pregnancy [1].

The diagnosis of EP in patients presenting with OHSS could be difficult due to enlarged ovaries especially if combined with increased BMI. In a case of primary ovarian pregnancy, localization of the ectopic embryo was achieved by TVS but only after filling the lower pelvis with saline solution [11]. By contrast, in a difficult case of primary abdominal pregnancy diagnosis was established four weeks after hospital discharge and after aspiration of 2000 ml of ascitic fluid by transabdominal paracentesis [12]. In our case, the ectopic gestation was originally missed by performing only transabdominal scan and contemplating that the patient suffered only from OHSS syndrome. The simultaneous presence of EP and OHSS was ascertained soon after by TVS performed by a specialist. In using TVS, it is important to follow a strict technique starting with the visualization of the cervix, endometrial cavity, lateral horns and then passing to the adnexes and the pouch of Douglas [19].

Cases of coexisting ovarian hyperstimulation and ectopic pregnancy, the most serious complications arising

from IVF treatment, are rare and pose a difficult diagnostic problem. Mild OHSS is fairly common, while severe OHSS may prove to be life threatening. In general, the management of ectopic pregnancies could be surgical or expectant in selected cases [20], while medical treatment with methotrexate is considered a bias bearing in mind the likelihood of a simultaneous endometrial (heterotopic) pregnancy. Surgical excision by the laparoscopic approach or by laparotomy is decided based on the patient's clinical status and wishes, the site of the ectopic embryo, the grade of OHSS and the time of diagnosis onset.

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