Heterotopic pregnancies in an in-vitro fertilization program

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Summary: During a four-year period in vitro fertilization (IVF) was carried out in 2,356 cycles. The pregnancy rate per transfer was 24% while the incidence of ectopic pregnancies was 7.5% per pregnancy. There were seven cases of heterotopic pregnancies – simultaneous intra- and extrauterine pregnancies (1.5% among all IVF pregnancies). Two of them were diagnosed after tubal rupture of the ectopic pregnancy and five cases were diagnosed by ultrasound at the 7th or 8th week of gestation. Laparotomy and subsequent salpingectomy was carried out in six cases while in one case the ectopic pregnancy was removed by laparoscopy. Three out of the seven heterotopic pregnancies (43%) were successfully continued with normal intrauterine embryo development and delivery.

Key words: Heterotopic pregnacies; In-vitro fertilization.

INTRODUCTION

The incidence of heterotopic pregnancy, a combined intra- and extrauterine pregnancy is not uncommon among patients treated by in-vitro fertilization (IVF) and embryo transfer (ET). A number of heterotopic pregnancies and the follow-up has been reported ([1, 2, 3, 4, 5, 6]).

The importance of close monitoring of all IVF pregnancies after repeated β-HCG measurements and transvaginal ultrasound until the 7th week of gestation is discussed.

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CASE REPORTS

Between August 1989 and August 1993, 2,356 oocyte retrievals were performed resulting in 1,915 embryotransfers. The outcome of these transfers was 461 pregnancies (24% pregnancy rate per transfer) 35 of which were ectopic and 7 heterotopic, respectively (frequency 1.5% among all IVF pregnancies). The patients underwent an ovarian hyperstimulation for the purpose of IVF with GnRH-analogues, HMG, pure-FSH and HCG. The age of the patients with heterotopic pregnancies, he history, the protocol for IVF and the number of oocytes retrieved and transferred are shown in Table 1.

Case No 1.

The patient had two ectopic pregnancies in her past history on the right tube. A heterotopic pregnancy was diagnosed after rupture of the ectopic pregnancy in the 7th week and re-

Table 1. — *Characteristics of patients diagnosed with heterotopic pregnancy and in vitro fertilization outcome.*

Patient	Age	Prior surgery*	Ovulation induction	Oocytes	ET**
1	30	R 2 Ectopics	10 Amp FSH, 34 Amp HMG	10	5
2	35	R, L closed	6 Amp FSH, 14 Amp HMG	17	5
3	35	R Salpingectomy	28 Amp HMG	5	4
4	34	R, L Hydrosalpix	6 Amp FSH, 28 Amp HMG	8	6
5	30	L Tube closed	6 Amp FSH, 20 Amp HMG	7	6
6	36	R Salpingotomy	6 Amp FSH, 22 Amp HMG	9	5
7	28	R Hydrosalpix	6 Amp FSH, 20 Amp HMG	7	5

(*) R: right tube, L: left tube; (**) embryo transfer.

moved by laparotomy; the intrauterine pregnancy ended in miscarriage after the procedure.

Case No 2.

The patient had a moderate hyperstimulation after superovulation complaining of lower abdominal pain while intraperitoneal fluid and large ovarian cysts were visualized by ultrasound. Upon detection of the intrauterine pregnancy by transvaginal ultrasound, enlarged ovaries and intraperitoneal fluid was also found which was aspirated twice; an ectopic pregnancy was not detected. At the 7th week she was transferred and collapsed at the clinic where laparotomy revealed a ruptured left ampullary pregnancy. The intrauterine pregnancy ended in miscarriage.

Case No 3.

Heterotopic pregnancy was suspected since β-HCG levels were assessed for a twin pregnancy on the 27th day post embryotransfer 17,450 IU) and only one intrauterine sac was visualized on ultrasound. Repeated ultrasound monitoring revealed the ectopic pregnancy on the left tube which was removed by laparotomy followed by salpingectomy (Fig. 1). The intrauterine pregnancy progressed satisfactorily with delivery of a normal male infant.

Case No 4.

The patient was treated by endoscopic surgery after ultrasound detection of a heterotopic pregnancy. The unruptured ectopic pregnancy was removed using bilateral cautery. The intrauterine pregnancy was aborted.

Case No 5.

Heterotopic pregnancy was suspected since β-HCG was elevated on the 27th day post embryotransfer (32014 IU) and only one intrauterine sac was visualized on ultrasound. Repeated ultrasound monitoring revealed an ectopic pregnancy on the left tube which was removed by laparotomy followed by salpingectomy. The intrauterine pregnancy progressed and ended satisfactorily.

Case No 6.

The patient had a severe hyperstimulation syndrome with enlarged ovaries and intraperitoneal fluid. Heterotopic pregnancy was not suspected because of normal β-HCG levels for a single pregnancy (5,400 IU on the 27th day post embryotransfer). An ultrasound in the 8th week revealed an ectopic pregnancy on the right side and blood in the Douglas pouch. Laparotomy was performed with salpingectomy. The intrauterine pregnancy progressed and ended satisfactorily.

Case No 7.

Heterotopic pregnancy was suspected due to high levels of β-HCG on the 15th (2,600) and 18th (11,000) day post embryotransfer. Ultrasound scanning revealed only one intrauterine gestational sac while extrauterine sacs were visible on both tubes. After the laparotomy on the 7th week with subsequent salpingectomy on both sides the intrauterine pregnancy ended in miscarriage.

DISCUSSION

The simultaneous appearance of an extrauterine and intrauterine pregnancy after in vitro fertilization seems to be a very rare phenomenon. The frequency of heterotopic pregnancy is reported to be 1% to 2.9% among all IVF pregnancies [3, 6, 7, 8].

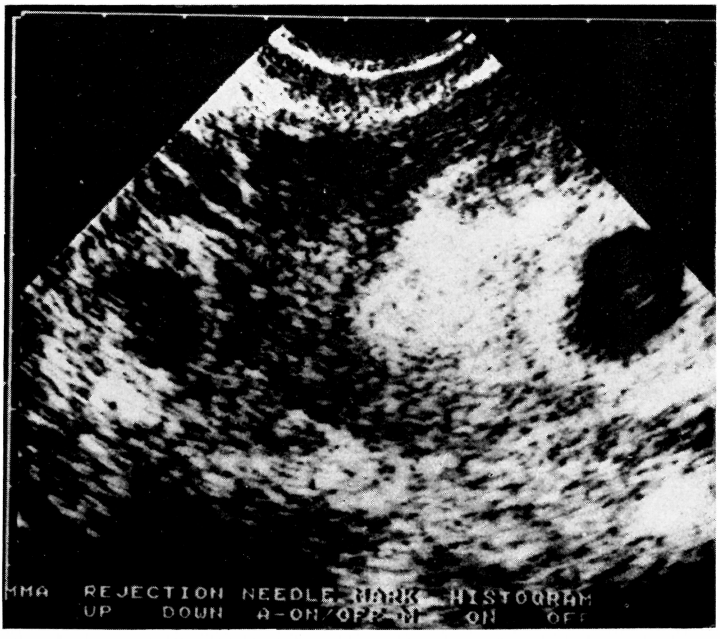

Fig. 1. — Transvaginal ultrasound of heterotopic pregnancy. Two gestational sacs are seen: (*a*) intrauterine with very thick endometrial appearance around the sac and (*b*) extrauterine on the left side.

In contrast to extrauterine pregnancies, heterotopic pregnancies are not easy to detect. Heterotopic pregnancies should be suspected in cases with high β-HCG levels suggesting a multiple pregnancy and when only one intrauterine gestational sac can be detected after trans-vaginal ultrasound scanning.

Damaged fallopian tubes after previous surgery and the transfer of more than one

Table 2. — *Diagnosis and treatment of heterotopic pregnancy.*

Patient	Diagnosis	Treatment	Intrauterine pregnancy
1	After rupture	Laparotomy	Missed abortion
2	After rupture at laparotomy	Laparotomy	Missed abortion after rupture of the ectopic
3	On ultrasound before rupture	Laparotomy	Delivery
4	On ultarsound before rupture	Endoscopic surgery	Missed abortion after laparoscopy
5	On ultrasound before rupture	Laparotomy	Delivery
6	On ultarsound before rupture	Laparotomy Laparotomy	Delivery Missed abortion
7	On ultrasound before rupture	one ectopic L one ectopic R	

embryo are factors which may contribute to the occurrence of heterotopic pregnancies [4, 5, 8, 9].

The way of embryo transfer, the depth at which the catheter is inserted into the uterine cavity and the position of the patient after embryo transfer have also been mentioned by other Authors as possible factors responsible for ectopic pregnancies [3, 4, 8, 9].

Early ultrasonographic diagnosis of an heterotopic pregnancy is very difficult if there are hyperstimulation signs like enlarged ovaries or intraperitoneal fluid, which may obscure both tubes. Laparotomy or endoscopic surgery were the treatment methods in the seven cases reported above (Table 2). Laparotomy had better results for the intrauterine pregnancy. In three cases removal of the extrauterine pregnancy allowed continuation of the intrauterine pregnancy.

Irrespective of the mode of treatment early diagnosis remains the most critical step in heterotopic pregnancy.

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