CASE REPORT

Combined intra-uterine and extra-uterine pregnancy associated with mild hyperstimulation syndrome after clomiphene ovulation induction

R.Thakur1 and M.El-Menabawey
Department of Obstetrics and Gynaecology, General Hospital, Hartlepool, Cleveland, UK
1To whom correspondence should be addressed

We report a combined intra-uterine and tubal pregnancy associated with mild ovarian hyperstimulation syndrome (OHSS) following ovulation induction by clomiphene. The diagnosis of ectopic pregnancy was originally missed until rupture occurred. OHSS confused the clinical picture, the important diagnostic feature being the fall in the haemoglobin concentration. The patient had a left partial salpingectomy and the uterine pregnancy progresses normally.

Key words: clomiphene/ectopic pregnancy/heterotopic pregnancy/mild OHSS

Case Report

A 30 year old woman presented to the Accident and Emergency Department, Hartlepool General Hospital, UK, with a 3 day history of lower abdominal discomfort and nausea of gradual increasing severity. Her last menstrual period had been 9 weeks previously. She had had one term pregnancy, delivered by lower segment Caesarean section 3 years previously because of breech presentation. She had been trying to conceive for the previous 2 years and had been referred to the Assisted Conception Clinic 9 months previously. She had received clomiphene 100 mg daily on days 2–6 of the cycle for the previous 5 months. On examination, her pulse rate was 90 beats per minute and regular; her blood pressure was 120/70 mm Hg. The abdomen was slightly distended with a moderate amount of tenderness and guarding. On speculum examination there was no evidence of vaginal bleeding. The cervix appeared normal. There was marked cervical excitation and tenderness in the fornices. It was difficult to assess accurately the size of the uterus but it appeared to be slightly enlarged. The pregnancy test was positive; her haemoglobin concentration was 10.2 g/dl and the haematocrit 0.302. The ultrasound scan showed a viable intrauterine pregnancy of 8 weeks duration. Both ovaries were enlarged with multiple cysts and there was free fluid in the Pouch of Douglas.

Since ovulation had been induced by clomiphene and the ultrasound scan showed an intrauterine pregnancy with multiple ovarian cysts and free fluid in the Pouch of Douglas, the patient was diagnosed as suffering from ovarian hyperstimulation syndrome (OHSS). The following day there was no improvement in her symptoms. Her haemoglobin concentration had dropped to 8 g/dl. A repeated estimation gave a haemoglobin concentration of 7.3 g/dl and an haematocrit of 0.214. There was an increasing tachycardia to 116 beats per minute and the blood pressure dropped to 70/50 mm of Hg.

The gradual fall in the haemoglobin concentration was incompatible with the initial diagnosis of OHSS. Bleeding from the ruptured ovarian follicle was suspected or alternatively, the possibility of concomitant ectopic pregnancy. An emergency laparoscopy was carried out. Blood was present in the Pouch of Douglas. The uterus was evenly enlarged, consistent with an 8 week intra-uterine pregnancy. Both ovaries were enlarged with multiple cysts and there was no haemorrhage from the ovaries. There was a ruptured left ampullary tubal pregnancy. Through a transverse suprapubic incision the pelvic organs were inspected and laparoscopic findings were confirmed. A left salpingectomy was carried out. The patient required a blood transfusion.

The ultrasound scan was repeated on the fourth post-operative day which confirmed a viable intrauterine pregnancy with a crown–rump length of 19.3 mm; equivalent to 8 weeks ± 4 days duration. The histology report on the salpingectomy specimen confirmed the diagnosis.

Discussion

Heterotopic pregnancy is defined as the simultaneous occurrence of an intrauterine and ectopic pregnancy. In a spontaneous conception, heterotopic pregnancy is a rare event. The risk of heterotopic pregnancy in spontaneous cycle varies between 1.30 000 (DeVoe and Pratte, 1984) and 1:15 000 (Winer et al., 1961). This figure is probably an underestimate and the incidence could be as high as 1:2600 (Bright and Gaup, 1990). The risk of ectopic pregnancy increases after pelvic inflammatory disease, mainly after Chlamydia infection (Brunham et al., 1986) and the widespread use of intra-uterine contraceptive devices (Russell, 1987). Microsurgical repair of the Fallopian tube damaged by pelvic inflammatory disease is considered to be a serious risk factor (Lavy et al., 1987). In cases of assisted conception such as in-vitro fertilization (IVF) with embryo transfer or gamete intra-Fallopian transfer (GIFT), the incidence of ectopic pregnancy is increased many times and a mean rate of 5% has been reported (Yorich et al., 1985). The incidence of combined pregnancy following IVF and embryo transfer is very high and has been reported to be 0.93% (Molloy et al., 1990), 0.9% (Dor et al., 1991) and 2.9%...
(Dimitry et al., 1990). The increase in the risk is due to ovulation induction leading to multifollicular development and multiple embryo transfer. The occurrence of heterotopic pregnancy after IVF is mostly due to tubal pathology (Dor et al., 1991). There is also a suggestion that high oestrogen concentrations after ovulation induction might disturb the tubal transport (Yovich et al., 1984; Molloy et al., 1990). Clomiphene, which increases the rate of twinning, could be associated with a heterotopic pregnancy rate of 1:900 (Bello et al., 1986).

Heterotopic pregnancy is a life-threatening condition. In an isolated ectopic pregnancy sonographic evidence of an empty uterine cavity combined with a β human chorionic gonadotrophin (HCG) concentration of >15 000 mIU/ml is the principal indicative factor (Wiedemann et al., 1989). In the case of combined intrauterine and extrauterine pregnancy the early diagnosis of ectopic pregnancy is almost impossible. The task becomes even more difficult when combined pregnancy is associated with OHSS because adequate visualization of adnexal region by sonogram is compromised. Clinical symptoms such as lower abdominal pain are also misinterpreted as arising from OHSS. Therefore it is not surprising that most heterotopic pregnancies are only diagnosed following rupture and haemorrhagic shock (Dimitry et al., 1990; Li et al., 1992). Considering the seriousness of the condition, the possibility of ectopic pregnancy must always be considered and a diagnostic laparoscopy should be performed whenever a diagnosis remains unclear. In the index case, rupture occurred 56 days after conception. In heterotopic pregnancy, despite the tubal rupture and haemorrhagic shock, the prognosis for the intrauterine gestation is good (Li et al., 1992) and ongoing pregnancy rates of 75.6% were reported by Reece et al. (1983) and 60% by Molloy et al. (1990). In the index case the pregnancy is progressing normally and revealed a normal development by sonogram.

References
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