CASE REPORT

Successful in-vitro fertilization in a natural cycle after four previously failed attempts in stimulated cycles

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A case is reported of successful in-vitro fertilization (IVF) and pregnancy in a natural cycle after four previously failed attempts with stimulated cycles. The patient began treatment at the age of 36 years and underwent four stimulated IVF cycles, each time with three embryos of good quality transferred. In one attempt, three cryopreserved embryos were transferred in a natural cycle. The patient failed to conceive. At the age of 38 years, the patient was entered into a natural cycle IVF programme. The patient conceived twice in each of her first two attempts but unfortunately aborted. In her third natural cycle of IVF, again with one oocyte obtained and one embryo transferred, the patient conceived and had a full term gestation. It is concluded that IVF in a natural cycle is a viable option for infertile women with blocked Fallopian tubes who have normal ovulatory menstrual cycles.

Keywords: IVF/natural cycle/tubal

Introduction

The first successful in-vitro fertilization (IVF) was performed in the natural cycle of an infertile woman with a tubal factor (Steptoe and Edwards, 1978). As this success could not be repeated by other groups (Johnston et al., 1981; Jones et al., 1982), IVF in a natural cycle was soon abandoned in favour of stimulated IVF. Stimulated IVF increases the probability of obtaining more than one fertilizable oocyte as well as that of conception. However, improvements in laboratory techniques and methods of follicle aspiration have created a renewed interest in natural cycle IVF and turned it into a viable option. We present the case of a patient with secondary infertility due to a tubal factor who failed to conceive during four stimulated IVF attempts despite good oocyte recovery, fertilization rate and embryo quality with even the possibility of cryopreservation. Subsequently, three pregnancies were achieved with natural cycle IVF of which two ended in a miscarriage and the last one resulted in the term delivery of a healthy child.

Case report

At the age of 36 years, the patient was admitted to our IVF department. She had undergone a bilateral tubectomy because of repeated ectopic pregnancy in the left tube and a haematosalpinx on the right side. A general examination revealed no abnormality. Her menstrual cycle was regular every 30 days. The patient requested IVF. In the first treatment ovarian stimulation was performed with the combination of a gonadotrophin-releasing hormone (GnRH) agonist (buserelin; Hoechst, Hoevelaken, The Netherlands) 3×2 inhalations/day starting on day 2 and human menopausal gonadotrophin (HMG) (Pergonal®; Serono, Den Haag, The Netherlands) 150 IU i.m. from day 3 onwards. Ovulation was induced with 10 000 IU human chorionic gonadotrophin (HCG) (Profasi®; Serono) when at least half of the number of follicles had a diameter of 18 mm and when serum 17β-oestradiol concentration was >1500 pmol/l (conforming to our standard protocol). Ovum retrieval took place on day 11. Eighteen oocytes were obtained and 10 fertilized. Three 4-cell embryos with score 1 (on scale 1 = high to 4 = low) were transferred 2 days later. The patient did not become pregnant. During the following 18 months, three further consecutive IVF attempts were performed with a so-called long protocol. Each attempt resulted in a good oocyte harvest (5, 22 and 16 respectively) and number of embryos (5, 13 and 11). Each time three embryos of good quality were transferred and in one attempt supernumerary embryos were cryopreserved and three were transferred in a later spontaneous cycle. The patient again failed to conceive.

In the meantime, a study protocol had been started in our centre for IVF in natural cycles. Women aged ≤38 years and with a history of secondary tubal infertility and regular menstrual cycles could participate. This patient was eligible and willing to participate. A baseline ultrasound scan on day 2 of menses was performed to exclude ovarian cysts, and a blood sample was drawn to determine a baseline follicle stimulating hormone (FSH) value. Serial transvaginal ultrasound and serum oestradiol plus luteinizing hormone (LH) concentration determinations were started on day 10. Follicular diameter was established by calculating the mean value of the two largest measurements perpendicular to each other. Subsequently, the patient was seen every other day until the leading follicle reached a diameter ≥13 mm. From then on the patient was monitored every day. When the follicular diameter reached >18 mm and the morning serum LH was <15 IU/l, the ovulation was triggered with 10 000 IU HCG between 23.30 and 24.00 h on that day (De Laurets et al.,...
Vaginal oocyte retrieval was scheduled 35 h later. Only the dominant follicle was aspirated. We failed to obtain an oocyte during the first three cycles. As the patient was very eager to continue, a new attempt was started. At the fourth cycle we succeeded in obtaining an oocyte, which was fertilized. Two days later we transferred a 4-cell embryo with score 1. Early testing for serum HCG, 15 days after oocyte retrieval, confirmed pregnancy. An ultrasound performed 33 days after ovum retrieval revealed an intrauterine pregnancy with a crown–rump length (CRL) of 4.3 mm and fetal heart beat of 108/min. This pregnancy ended in a miscarriage at a gestational duration of 8 weeks and 5 days. The patient started a new attempt a few months later. The protocol was not changed. Again we obtained one oocyte and transferred a 4-cell embryo score 2. The patient became pregnant again, but unfortunately this pregnancy ended also in a miscarriage at a gestational age of 8 weeks. Nevertheless, the patient was very eager to continue IVF treatment in a natural cycle and started again. This sixth attempt proceeded smoothly. During the whole period the patient was treated, no changes were made in laboratory methods, oocyte retrieval or embryo transfer techniques. The patient became pregnant once more. The first ultrasound performed at a gestational term of 6 weeks and 2 days showed an intrauterine pregnancy with a CRL of 3.2 mm and positive heart beat. Ultrasound examination at 8 and 10 weeks revealed normal progress. Amniocentesis was performed between 14 and 15 weeks gestation. The fetal karyotype was reported to be normal 46,XX, and the α-fetoprotein value was within normal limits. The patient delivered a healthy daughter after an uncomplicated pregnancy at a gestational term of 42 weeks.

Discussion

IVF in a natural cycle is a viable option for infertile women with a tubal factor provided they have regular ovulatory cycles. The timely retrieval of the mature oocyte is a critical factor involved in the success of the procedure. Although the use of HCG allows for accurate timing and scheduling of oocyte retrieval, there will be a number of retrieval attempts which fail to obtain an oocyte. This is because there is no single, completely reliable, parameter for ovulation prediction and because there is large variation in hormonal and clinical parameters predicting ovulation even in the same patient (Garcia et al., 1981). For this patient we failed to obtain an oocyte in the first three attempts while, after applying the same protocol, we were successful in the three subsequent cycles. The probability of obtaining an oocyte is the same in each cycle as long as the protocol is not changed. Another problem which can occur in natural cycle IVF is cancellation of the treatment due to an untimely LH surge. The use of GnRH antagonists may prove helpful in reducing spontaneous LH surges during natural cycles (Rongières-Bertrand et al., 1999).

The patient conceived each time after the embryo transfer in natural cycle IVF but, despite the transfer of comparable quality embryos, she never conceived in stimulated IVF. The first explanation might be that of a coincidence. However, the endometrium in natural cycle IVF is spared from the adverse effects associated with ovarian stimulation (Fossum et al., 1989; Paulson et al., 1990) and as such might be the explanation for the success.

Natural cycle IVF is a low-cost and low-risk treatment, easy to perform, comfortable for the patient and it can be repeated on a monthly basis, therefore increasing the overall chance of success. Other authors have used natural cycle IVF as a good model for assessing fertilization and embryo development under spontaneous conditions (Zayed et al., 1997), or as a good alternative for stimulated cycles in poor responders (Bassil et al., 1999). Encouraging results have been obtained. To establish whether it makes sense to offer natural cycle IVF to infertile patients with tubal pathology as a regular treatment, a prospective, randomized study comparing natural cycle IVF and stimulated IVF is required.

References


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