CASE REPORT

Astonishing fertility from a single oocyte recovery

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A 36 year old patient underwent in-vitro fertilization (IVF) and embryo transfer. Three embryos were transferred to her uterus and eight spare embryos were cryopreserved. The patient conceived a quadruplet pregnancy and delivered two boys and two identical twin girls by Caesarean section at 30 weeks gestation. The couple subsequently donated their cryopreserved embryos to the embryo donation programme for the use of other couples. Two agonadal patients received these cryopreserved-thawed embryos, each in a hormone replacement cycle. Both conceived, one has safely delivered twins and the other conceived a twin pregnancy, one of the fetuses has vanished and the other is progressing normally. The overall embryo implantation rate was seven out of nine (78%).

Key words: agonadal/cryopreservation/embryo donation/IVF

Introduction

In-vitro fertilization (IVF) with embryo transfer has resulted in a substantial increase in the incidence of multiple pregnancy, with its associated increased risk of maternal and fetal complications. Limiting the number of embryos to be transferred and cryopreserving spare embryos helps to decrease the risks and maximise the chance of conception. Trounson et al. (1983) reported the first human pregnancy after the transfer of a donated embryo and Lutjen et al. (1984) reported the first birth after oocyte donation in a patient with primary ovarian failure. Since then Serhal and Craft (1989), Antinori et al. (1993) and Sauer et al. (1995) have shown that women in their late 50s and older, can establish successful pregnancies and that the uterus of a menopausal woman can respond to steroid therapy and enable embryos to implant as efficiently as in the uterus of a young woman.

Case report

A 36 year old patient with a 15 year history of primary infertility due to tubal damage was referred to Bourn Hall Clinic for IVF and embryo transfer. The couple had previously had six unsuccessful IVF/embryo transfer treatments at another centre using clomiphene citrate and human menopausal gonadotrophins. The number of oocytes retrieved varied between two and six, the number of embryos transferred varied between two and four and the patient received natural progesterone for luteal phase support. Three years after her last IVF attempt the couple underwent an attempt at IVF at Bourn Hall Clinic, using a long gonadotrophin-releasing hormone (GnRH) agonist combined with gonadotrophin protocol (Marcus et al., 1993). A total of 15 oocytes were retrieved by transvaginal follicular aspiration and 11 oocytes fertilized. Three good quality embryos were transferred to the uterus and the eight remaining embryos were cryopreserved (Testart et al., 1986; Sathanandan et al., 1992). The patient received natural progesterone for luteal phase support. High serial plasma human chorionic gonadotrophin (HCG) concentrations from day 13 after embryo transfer suggested a multiple pregnancy. A transvaginal ultrasound scan on day 33 after embryo transfer identified four intrauterine gestation sacs, each containing a fetus with visible cardiac activity. The crown-rump lengths were compatible with dates. The couple received counselling about the obstetric risk of a quadruplet pregnancy but decided to continue without interference. Follow-up scans at 10 and 18 weeks showed normal fetal growth and development. The pregnancy progressed uneventfully till 29 weeks and 5 days gestation, when the membranes ruptured spontaneously. Corticosteroids were administered and lower segment Caesarean section was performed at 30 weeks gestation. Four babies were delivered, two boys and two girls whose weights were: 1.304, 1.190, 1.134 and 800 g respectively; all were alive and well. The two girls were identical twins.

The couple subsequently donated their eight spare cryopreserved embryos. They received counselling and underwent routine screening. Two couples received the embryos. The first recipient (A) was a 41 year old woman and the second recipient (B) was 46 years old. Both suffered from premature menopause. The partner of patient A suffered from severe oligozoospermia and patient B's husband suffered from azoospermia due to primary testicular failure. Four embryos were thawed on each occasion, all four survived the thawing and three good quality embryos were transferred transcervically into the uterine cavity in a hormone replacement cycle (HRT) in each recipient. The fourth embryo was not suitable for re-freezing and was discarded. Patient A had her embryos transferred in August 1995 and patient B had three embryos transferred in March 1996. Both recipients conceived. Recipient A had an uneventful pregnancy and delivered twin live births, a boy and a girl, at 34 weeks gestation weighing 1.980 and...
transferred were high at 66.7%. This provides further evidence that the uterus can respond very quickly to steroid hormones after a long period of amenorrhoea and is capable of implanting embryos after many years of post-menopausal amenorrhoea.

The astonishingly high implantation rate from a single oocyte recovery from a donor aged 36 provides further evidence that oocyte quality does not decline with increasing maternal age

References


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Discussion

Camus et al. (1986) reported a quadruplet pregnancy after the replacement of three embryos after IVF with embryo transfer, their patient had a Caesarian section at 35 weeks gestation and four healthy babies, three boys and a girl were born. Although the obstetric outcome of triplet and quadruplet pregnancies is often poor, fortunately, our patient's outcome was satisfactory. Selective fetal reduction of high order multiple pregnancies has been proposed as an alternative in order to increase the chances of survival of the remaining fetuses. However, this procedure creates a number of ethical and medical concerns. Critics of the management of this case will say only two embryos should have been replaced in this patient. It would have been difficult to persuade this couple to accept this because of her age, their 15 year history of infertility, their six previous failed attempts at IVF and embryo transfer, and no family history of high fertility. This case shows that, even by limiting the number of embryos transferred, there may still be an unexpected high order multiple pregnancy. Edwards et al. (1984) first reported an increased incidence of identical twins following IVF (nine out of 600; 1.5%). Derom et al. (1987) then reported a 1.2% incidence of monozygotic twins after artificial induction of ovulation, compared with 0.45% in the general population. The exact mechanism is not fully understood but it could be due to a hardened zona pellucida causing embryo splitting during hatching.

This case report illustrates the immense value of embryo cryopreservation as an integral part of an IVF programme. The indications for embryo cryopreservation are: freezing spare embryos for future embryo transfer; when there is a high risk of developing ovarian hyperstimulation syndrome; and when fresh embryo transfer would be undesirable, such as suboptimal endometrial development, the presence of endometrial polyps or if the patient's health is not good. We have previously shown that there is no relationship between the length of storage of cryopreserved embryos and pregnancy rates (Avery et al., 1995), no difference between the outcome of children born as a result of fresh and cryopreserved-thawed embryo transfers (Wada et al., 1994), and no difference in the success of fresh and cryopreserved embryo transfer (Brinsden et al., 1991) The first birth after cryopreservation was twins conceived by the team of Zeilmaker et al. (1984).

Following the reports of Trounson et al. (1983) and Lutjen et al (1984) on the first pregnancies following embryo and oocyte donation, it has become clear that the state of menopause does not prevent successful pregnancies being established. More reports have appeared (Antinori et al., 1993; Borini et al., 1995; Sauer et al., 1995) showing that patients in their late 50s and even 60s can establish pregnancies. Their fertility is high, with embryo implantation rates similar to women in their early 30s and with low abortion rates. Neither patient A nor patient B received any preparatory cycle of HRT prior to their transfer cycles and their implantation rates per embryo

2.250 g. Recipient B conceived a twin pregnancy, one of the fetuses 'vanished' at 8 weeks and she has an ongoing singleton pregnancy.