CASE REPORT

Three blastocyst stage embryo transfer resulting in a quintuplet pregnancy

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High-order pregnancies are associated with high morbidity and mortality and the incidence is increased as a drastic complication of assisted reproductive technology. This case presents a high-order pregnancy achieved by transfer of three blastocyst stage embryos resulting in a quintuplet pregnancy including a monochorionic triplet. Following the selective termination of the monochorionic triplet, two healthy children were born. The mechanism of monochorionic development and its association with assisted reproductive technology are discussed.

Key words: blastocyst transfer/ICSI/multiple pregnancy/ovarian stimulation/quintuplets

Introduction

The success of assisted reproductive techniques is complicated by the increase in the rate of high-order multifetal pregnancies. The improvement of culture media and availability of blastocyst transfers may help to preserve the rate of clinical pregnancies achieved by assisted reproductive techniques, while decreasing the risk of multiple pregnancies. Monozygotic multifetal pregnancy is associated with severe complications due to vascular anastomoses, causing twin-to-twin transfusion. Multifetal pregnancy reduction (MPR) is an inevitable invasive procedure to reduce the risk of forthcoming complications. This report presents a case of conception after intracytoplasmic sperm injection (ICSI) and transfer of three blastocyst stage embryos leading to a quintuplet pregnancy, and the subsequent delivery of two healthy babies following the selective reduction of the monozygotic triplet in her quintuplet pregnancy.

Case report

The patient was a 34 year old woman who complained of primary infertility for 11 years. She had had a regular menstrual history. The physical and gynaecological examinations as well as the laboratory and radiological studies revealed no abnormal findings. Her husband had been operated for a varicocele on the left side. The semen analysis revealed severe oligoasthenoteratozoospermia (concentration: \(2 \times 10^6/ml\), total motility: 13% (5% progressive motility, morphology according to Kruger’s strict criteria: 2). His peripheral karyotype was 46XY and fluorescent in-situ hybridization analysis for Y microdeletions revealed negative findings. The couple was signed for ICSI treatment and gonadotrophin-releasing hormone analogue (Buserelin, Suprefact®; Hoechst AG, Frankfurt, Germany) was started during the midluteal phase in a long protocol manner. The ovarian stimulation was performed with the combination of FSH (MetrodinHP®; Ares Serono Laboratories, Welwyn Garden City, Herts, UK) and human menopausal gonadotrophin (HMG, Pergonal®; Ares Serono), starting with 150 IU of each hormone and adjusting the dose in a step-down fashion. Human chorionic gonadotrophin (HCG, 10 000 U; Profasi®; Ares Serono) was given to trigger ovulation. The total duration of induction was 13 days and HCG was given when the serum oestradiol concentration was 1910 pg/ml. A total of 13 oocytes were retrieved and nine were classified as metaphase II oocytes. ICSI was performed and seven two-pronuclear pre-embryos were achieved. The embryos were cultivated in vitro until the blastocyst stage within sequential medium (G1, G2; IVF Scandinavian, Gothenburg, Sweden). Considering the patient’s age, one 4AA and two 3AA blastocysts were transferred without assisted hatching. The patient was given 100 mg progesterone i.m. beginning from the next day of oocyte retrieval until the serum β-HCG assay, 12 days after the embryo transfer. Two consecutive β-HCG analyses revealed 617 and 1147 mIU/ml. Three weeks after the embryo transfer, transvaginal ultrasonography was performed and a quintuplet pregnancy was observed. Ultrasonographic examination revealed three gestational sacs including a monozygotic triplet and another diamniotic dichorionic twin (Figure 1). Fetal heart beats were detected in all. The potential risks of high order multifetal pregnancies as well as the benefits and risks of MPR were discussed with the couple. Following the informed
Discussion

Splitting of the zygote at various stages of development leads to monozygotic multiple pregnancies. The mechanism of monozygotic twinning is not well defined. Monozygotic multiple pregnancies following embryo transfers have been previously reported (Salat-Baroux et al., 1994; Balaisch-Allart et al., 1995; Peramo et al., 1999). The incidence of monozygotic twinning in spontaneous pregnancies is reported to be 1/250 and it is reported to be increased after ovulation induction and assisted reproductive techniques (Derom et al., 1987; Wenstrom et al., 1993; Alikani et al., 1994; Meldrum and Hamilton, 1996; Slotnick and Ortega, 1996). It is not clear whether the ovulation induction itself, in-vitro conditions or the mechanical-chemical trauma to zona pellucida is responsible for the splitting. Controversy exists in the relation between zona manipulation and zygotic splitting (Blickstein et al., 1999; Sills et al., 2000). Animal studies have shown that mechanical cleavage of mammalian embryos in vitro could produce monozygotic twins (Ozil, 1983). Whether the increased risk incidence of monozygosity represents mono or dichorionic pregnancies or monoamniotic multiples awaits further studies. One would further expect an increase in the late splitting leading to an increase in the risk of conjoint twins which has not been demonstrated until now. In this particular case, the splitting might have occurred either in the blastocyst stage or at the bilaminar germ disc just before the appearance of the primitive streak. The latter is more probable because the embryo is evaluated just before the transfer and a single intracellular mass in the blastocyst had been confirmed.

High order pregnancies and, in particular, monozygotic twins or triplets, are associated with increased risk of maternal complications as well as a high prevalence of prenatal and neonatal morbidity and mortality. In addition, the perinatal mortality rate was reported to be as high as 41.6% in sextuplets, 21.9% in quintuplets, 20% in quadruplets and 16.4% in triplets (Kanhai et al., 1986; Botting et al., 1987; Kahraman et al., 1997). Multifetal pregnancy reduction is an effective method to decrease miscarriage rate and perinatal mortality (Evans et al., 1993; Mansour et al., 1999). This is particularly true regarding quadruplets and quintuplets. However, there is controversy for the reduction of triplets to twins. Rate of prematurity and low-birthweight infants were found to be lower in triplets reduced to twins, when compared with triplets managed expectantly (Lipitz et al., 1994; Boulot et al., 2000). On the contrary, Kadhel et al. reported that the mortality rate of triplets managed expectantly did not differ from that of triplets reduced to twins (Kadhel et al., 1998). In addition, MPR is not free from complications. The miscarriage rate due to selective reduction has been reported to vary from 0 to 40% (Sebire et al., 1997; Evans et al., 1993; Itskovitz-Eldor et al., 1992).

Development of high quality embryos and limiting the number of embryos transferred must be the prerequisites for assisted reproductive technology programmes. However, this would not work for monozygotic multiples since the mechanism itself has not been clarified yet. The incidence of monozygotic twins has been reported to be as high as 4.9% after single embryo transfer (Blickstein et al., 1999). Until satisfactory data have been gathered and the underlying mechanism for embryo splitting has been elucidated, every effort should be made to document these cases. Selective reduction is an alternative to avoid some complications, ethical dilemmas notwithstanding.

References


Figure 1. The quintuplet pregnancy including a monochorionic triplet (a) and two dichorionic twins (b and c).
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