Triplet pregnancy after oocyte donation in women 46 years of age and older: Three case reports

E. Makrakis[1], *M.D.*; M. Grammatis[1], *M.D.*; N. Vitoratos[2], *M.D.*; D. Stavrou[1], *M.D.*; P. Karantzis[1], *M.D.*; K. Pantos[1], *M.D.*

[1]Centre for Human Reproduction, Athens; [2]2nd Department of Obstetrics and Gynecology, University of Athens, Aretaieion Hospital. Athens (Greece)

Summary

Purpose: Presentation of three triplet pregnancies achieved in women 46 years of age and older with the use of donated oocytes.

Material & Methods: Two healthy perimenopausal women 46 and 48 years old and one healthy menopausal woman 48 years old, requesting fertility options. All of them followed oocyte donation programs resulting in triplet pregnancy. Maternal as well as perinatal complications, mode of delivery and birth weight are reported.

Results: Three triplet pregnancies were achieved using donated oocytes. Prenatal diagnosis was reassuring. Preterm rupture of membranes, preterm labor and gestational diabetes complicated the pregnancies. Cesarean section was the mode of delivery for all the cases giving birth to nine healthy neonates weighing between 1,130 and 2,450 g. No postpartum complications were encountered.

Conclusions: Triplet pregnancies achieved with the use of donated oocytes at a very advanced maternal age represent high-risk obstetrical cases. Cautious prenatal evaluation of maternal health and intensive antenatal surveillance are imperative principles allowing the most favorable outcome of these pregnancies.

Key words: ART; Oocyte donation; Triplet pregnancy; Advanced maternal age.

Introduction

Changes in social attitudes towards women's professional careers and parenting have resulted in an increasing demand for application of oocyte donation programs in perimenopausal and even menopausal women. Three cases of women 46, 48 and 49 years old participating in such programs, who achieved and delivered trichorionic-triamniotic triplet pregnancies, are reported. Cases like these (women > 45 years old who delivered triplets) have rarely been reported in the medical literature [1-4].

Case Reports

Case A: A 46-year-old woman married to a healthy 48-year-old male presented with secondary infertility. She had had two spontaneous conceptions ending as first-trimester miscarriages, eight and seven years before presentation, without further investigation. The couple had never stopped trying since then, without seeking expertise advice. She reported menstrual cycle irregularity of 3-years' duration, having only four periods in the previous 12 months. The value of her serum follicle stimulating hormone (FSH) was 27 mg/l whereas her husband's semen analysis was normal. The option of an oocyte donation program and the risks of a multiple gestation as well as those of a pregnancy in advanced maternal age were discussed with the couple. Their decision was positive and the candidate recipient went through complete health screening including cardiovascular, renal and liver function evaluation, which revealed no medical problems. Preparation of the recipient's uterus included administration of estradiol valerate in a dose of 2 mg daily initially. Seven days later, when the thickness of the endometrium was 6 mm, the dose was increased to 6 mg daily, and in a five-day period an endometrium of 10 mm was achieved. The recipient was synchronized with a donor's current cycle by adding 300 mg per os and 600 mg per vagina of progesterone on the day of donor oocyte retrieval. Using the recipient's husband sperm, four oocytes were fertilized and three day-2 embryos of fair to good (grade I and II) quality were transferred. Fourteen days later, the serum human β- chorionic gonadotrophin (bHCG) level was 2190 miu/ml and the four-week post-transfer ultrasound scan revealed three gestational sacs, each one with a fetal pole showing cardiac activity. The option of fetal reduction was offered and strongly recommended but the couple rejected it. The triplet pregnancy was mostly uneventful until the 31st week of gestation. A high protein diet as well as iron and folic acid supplementation was advised. A nuchal translucency scan at 11 weeks' gestation, amniocentesis at 16 weeks' gestation as well as a full anomaly scan at 20 weeks were reassuring. During the third trimester antenatal visits were organized once a fortnight, adequate bed rest was advised and serial ultrasound scans showed appropriate fetal growth. Maternal blood pressure, glucose screening and weight gain remained within the normal range. Starting on the 28th week 12 mg of beta-methasone were given intramuscularly once a week. During the 31st week, the pregnancy was complicated by premature rupture of membranes followed by signs of premature labor. Cesarean section was performed without delay giving birth to a male 1,405 g, a male 1,540 g and a female 1,595 g. The postpartum period was uneventful and the babies were discharged 26 days later with no complications.

Case B: A 48-year-old woman married to a 39-year-old healthy male presented with secondary infertility. She had had a spontaneous first trimester miscarriage eight years before and the couple had kept trying since then without seeking medical advice. Her previous gynecological history included laparoscopical diagnosis of mild endometriosis, 14 years before, followed by a six-month treatment with danazol. Her menstrual

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cycle had become irregular during the previous two years and her serum FSH value was 29 mg/l. The husband's semen analysis was normal. Consultation for oocyte donation, medical investigation, protocol for endometrial preparation and synchronization with the donor's current cycle were similar to case A. Five oocytes were fertilized using the husband's sperm and three day-2 embryos of good (grade I) quality were transferred. Fourteen days later the serum bHCG level was 2512 miu/ml and the four-week post-transfer ultrasound scan revealed three sacs and fetal poles with cardiac activity. Fetal reduction was not elected and the triplet pregnancy continued. Obstetric care and advice as well as application of prenatal diagnosis were similar to case A, the latter again being reassuring. Fetal growth was adequate and no complications were noted until the 27th gestational week, when mild gestational diabetes developed. The patient had appropriate diet-controlled glucose levels until the 35th week, when an elective Cesarean section was performed and she gave birth to three males weighing 2,450 g, 2,085 g and 1,614 g. The postpartum period was uneventful and the neonates were discharged after five, seven and 21 days, respectively.

Case C: A 49-year-old woman, married to a 57-year-old healthy male, presented with primary infertility. Her previous medical and gynecological history was unremarkable and she had become menopausal eight months before presentation (serum FSH value of 46mg/l). The couple had been trying to conceive for the previous three years. The husband's semen analysis was normal. Consultation for oocyte donation, medical investigation, protocol for endometrial preparation and synchronization with the donor's fresh cycle were similar to cases A and B. A first attempt, including fertilization of six oocytes and transfer of three day-2 embryos of good (grade I and II) quality, was unsuccessful. The second attempt included fertilization of five oocytes and transfer of three day-6 blastocysts resulting in a 14th day post-transfer bHCG of 2789 miu/ml. The 4-week post-transfer ultrasound scan confirmed three gestational sacs and three fetal poles with positive cardiac activity. Obstetric care and advice as well as application of a reassuring prenatal diagnosis were similar to cases A and B. No complications were noted until the 27th gestational week, when the patient was admitted due to signs of preterm labor. She was put on IV ritodrine and labor was arrested. Two days later she was discharged on oral ritodrine for one week. In the 31st gestational week she was re-admitted with regular contractions. A Cesarean section was performed resulting in the birth of a male weighing 1,450 g, and two females weighing 1,384 g and 1,130 g. The postpartum period was uneventful and the neonates were discharged after 26, 30 and 36 days, respectively.

Discussion

Attempting childbearing in advanced maternal age remains controversial [5, 6] and cases of women over 45 years old who have achieved pregnancy, especially multiples, using donated oocytes is worth close speculation. Points of interest in cases like these, include the following: a) advanced maternal age represents a serious risk factor associated with pregnancy complications [7, 8] and older women are more likely to already have other independent risk factors like essential hypertension, cardiovascular disorders, renal disorders, etc. b) assisted reproduction techniques, by means of oocyte donation, inherit the associated increase in multiple gestations, to that, already at risk, age group, adding another risk factor for obstetrical complications. Maternal morbidity as well as perinatal morbidity and mortality are increased in multiple gestations and the higher the order of multiples, the higher the risk of complications. c) It is obvious that the combination of these two independent factors (advanced maternal age and multiple pregnancy) results in a pregnancy at serious risk, and d) many studies have concluded that the inevitable 'aging' of the uterus does not affect the pregnancy rates when using donated oocytes in older women [9].

As the desire of older women for childbearing, not infrequently, overcomes the above-mentioned pregnancy risks, the only way to improve their outcome is to prevent and/or early detect any major obstetrical complications. This can be achieved with a cautious prenatal evaluation of maternal health followed by intensive antenatal surveillance. Women over 40 years old with ominous health problems, especially concerning the cardiovascular system and glucose metabolism, should definitely be excluded from ART programs. When a triplet or higher order pregnancy is established the option of fetal reduction should be strongly recommended; prenatal screening and application of techniques for prenatal diagnosis are imperative. Diet should be adapted to meet the increased requirements, antenatal appointments should be held by experienced staff and techniques for monitoring fetal well being should be applied after viability is achieved.

Applying the above rules to the cases presented in this manuscript contributed to the favorable observed outcome: no serious antenatal or postnatal complications were encountered and the nine neonates confronted no threatening problems.

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Address reprint requests to:
E. MAKRAKIS, M.D.
Centre for Human Reproduction
5, Kifisias av. Marousi
Athens 15123 (Greece)