Birth of Healthy Twins Resulting from Donated Oocytes and Posthumous Use of Frozen–Thawed Spermatozoa Obtained Prior to Chemotherapy

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The improvement in life expectancy, following better cancer therapy combined with new options in treating male infertility have increased the use of sperm freezing. We describe a rare case of twin pregnancy of a childless widow, using donated oocytes after ICSI with her deceased husband's banked frozen spermatozoa. Sperm was frozen before chemotherapy treatment and a written consent for future thawing and injection to donor oocytes was given. Use of thawed spermatozoa after death was not mentioned in the consent form. During the husband's illness years, ICSI of donated oocytes fertilized with thawed spermatozoa yielded three embryos, but no pregnancy was achieved after ET. While waiting for a subsequent oocyte donation, the male partner died of his malignancy. The woman expressed her wish to be treated with the frozen spermatozoa of her deceased husband. Since the original informed consent did not cover postmortem use of the husband's sperm, a special application for its use was made and subsequently approved by the Israeli Ministry of Health legal advisor. Another six donated oocytes were fertilized with the deceased's thawed spermatozoa, and the transfer of four embryos to the uterine cavity resulted in a twin pregnancy and later delivery of two healthy babies. This case emphasizes the importance of written informed consent signed by patients with a life-threatening disease at the time of banking spermatozoa, and discussing the possibility of its posthumous use. Several legal and ethical concerns are discussed.

KEY WORDS: chemotherapy; oocyte donation; posthumous reproduction; spermatozoa banking.

INTRODUCTION

The improvement in cancer treatment and life expectancy, combined with new male infertility treatment options, have increased the number of patients requesting sperm banking (1).

Requests have also been made to collect "fresh" spermatozoa from terminally ill or recently deceased males by various techniques for future use, as well as the posthumous use of thawed spermatozoa

collected and stored during life. This situation provokes questions concerning the rights of the recently deceased male, his wife, his family and even the future offspring (2).

CASE REPORT

A 38-year-old woman referred to our institute for egg donation after three unsuccessful IVF trials with extremely poor ovarian response and Day 3 serum FSH level of 28 IU/L. Seven years before her present admission, her husband was diagnosed with acute leukemia at the age of 54 years. Six sperm samples were cryopreserved, within an

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interval period of 2 weeks, before chemotherapy was initiated. Repeated semen analysis performed before cryopreservation revealed semen volume—3 mL (2–5 mL); pH 8.0 (7.2–8.3) and concentration ranging between few cells (three samples) and 0.1–0.4 million cells per milliliter (three samples). Three years hence, another IVF patient donated oocytes, which were injected with four thawed spermatozoa. Sperm parameters of the thawed spermatozoa before injection were sperm concentration—0.02 million per milliliter, and motility—50% grade I–II. The endometrium was hormonally prepared by prior daily administration of 4-mg estradiol valerate (Progynova, Schering AG, Berlin, Germany) for 12 days, upon achieving endometrial thickness of 9.1 mm. In addition, daily injections of progesterone BP 100/2 mL solv., ethyl oleate BP with 10% benzyl alcohol (Gestone 100, Paines & Byrne, Surrey, U.K.) were administered to mimic the luteal phase. Four embryos (2–5 cells) grade II and grade II–III, were transferred to the uterus of the patient. Unfortunately, the woman failed to conceive. At this time, the couple expressed their wish to continue to try to achieve pregnancy. Two years later, at age 42, the woman informed the medical staff that her husband had died of leukemia at the age of 59 years. Based on the previous detailed informed consent that had permitted insemination of frozen–thawed spermatozoa with donor oocytes during the husband's lifetime, since the use of his sperm after death was not previously prohibited and after counseling with the local and the general legal advisor of the Ministry of Health, permission was given for further ART trial. Six donated oocytes were injected with the deceased husband's thawed spermatozoa. Four embryos were transferred into the uterus of the patient 72 h after the injection, at 6–8-cell stage, using a Wallace catheter (Wallace Ltd., Colchester, U.K.).

A twin pregnancy was achieved. Pregnancy course was uneventful. Cesarean section was performed in active labor at 34 weeks of gestation for breech presentation of the first twin. Two male healthy newborns were delivered with similar birth weight of 1800 g.

DISCUSSION

According the regulations of the Israeli Ministry of Health, last revised in 1994, the use of donor spermatozoa for insemination is acceptable, and utilized clinically either in intrauterine inseminations or in IVF-ET, for single women or couples with male partner azoospermia. Moreover, when oocytes are not

available (advanced age or premature menopause), the use of donated oocytes and donor spermatozoa are also allowed after specific permission from the Ministry of Health.

The Israeli law concerning the storage of male spermatozoa before chemotherapy stipulates that spermatozoa may be stored for 5 years only, unless a written request for continuation of storage is filed. The same holds for sperm samples of a deceased husband, which would otherwise be destroyed after his death, unless a written request by his legal wife is received. In these cases, the widow should file special request within 1 year. There are no additional clauses in the Israeli law concerning the rights of any other person (including the family of the deceased), for or against posthumous use of spermatozoa.

In the current case, frozen spermatozoa were stored and already used to inseminate donor oocytes, when both partners were alive. The sperm bank staff had no information on the husband's death, until the widow expressed her wish for further treatment. The desire to use the deceased sperm instead of donor sperm was interpreted as an affirmation of mutual love and acceptance, and the woman's wish to carry her husband's genes for future generation, even after his death.

Recently, Belker *et al.* (3), raised arguments which both support and oppose sperm retrieval without advanced written directives from a moribund or a recently deceased man. They conclude that “although not absolutely precluded, postmortem use of frozen sperm in general is not to be encouraged, unless the will of the deceased to have such use, of his spermatozoa, be confidently concluded, and the well-being of any resulting new life is reasonably assured.”

The ethics committee of the American Society for Reproductive Medicine (ASRM) supported these conclusions which were published in 1997 ethical considerations regarding posthumous reproduction (Ethical considerations of ART) (4): “Programs are urged to insist that donors make their wishes known. If no decision on disposition after death has been made, one would expect that in most instances this would preclude any posthumous use. Sperm banks are not uniform in the way they deal with saving or discarding of samples from deceased donors, and a sperm bank may or may not know of a donor's death if all testing of the donor to exclude infection already have been performed.”

In principal, it is our task to assure that the use of an individual's spermatozoa will be in a manner consistent with his expectations during his life, as well as after death. The deceased patient gave the

permission for use of the frozen spermatozoa with donated oocytes in his lifetime. In fact, even though circumstances had changed, the use of the husband's thawed spermatozoa was according to his known wishes, and the legal advisor of the Israeli Ministry of Health honored these wishes. The ASRM committee commented that since the term "known wishes of the husband" could be interpreted in different ways "such requests pose judgmental questions, which should be answered within the context of the individual circumstances and applicable state law."

The ethics task force of the European Society of Human Reproduction (ESHRE) has not yet concluded its guidelines at this time, and allow use of gametes after death according prior informed consent of the husband (F. Shenfield personal Communication). It is illegal to store sperm, oocytes, or embryos in the U.K., without the written consent of their provider(s) (Human Fertilization and Embryology Act) (5).

The question as whether the family of the deceased male patient has the legal right to oppose the post-mortem use of sperm of their deceased relative is of importance. Fortunately in our case, the family of the deceased husband honored the widow's request and no conflict of interest has occurred. However, in terms of inheritance and legitimacy, a child born after man's death may not have similar rights compared with a child born to his father in his lifetime (6).

The concern about the welfare of the child, namely the ability of a single woman to raise twins without her

husband is also questionable (7). These psychological impacts on fatherless children are unknown, and no such differences are comprehended between use of deceased frozen spermatozoa versus frozen donor spermatozoa, for single-parent families.

We described a unique case of a widow having twins, originating from donated oocytes and prechemotherapy frozen stored semen of her deceased husband. There are very few case reports of posthumous use of spermatozoa to achieve pregnancy, no case of insemination of donor oocytes was previously published, and the complicated legal and ethical issues were discussed.

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