

Father-to-son sperm donation.

A report of three cases

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Summary

Sperm donation is a common practice in assisted reproduction. In cases of azoospermia and negative results of testicular sperm extraction, it appears as the only solution. Sperm donation entails a complete genetic dissociation between husband and offspring, which brings psychological stress for the couple arising from ethical and existential dilemmas. Faced with such dilemmas, some couples prefer father-to-son donation as an alternative solution. Here, three cases of non-obstructive azoospermia are presented where intracytoplasmic sperm injection was performed with father-to-son sperm donation.

Key words: Ethics; ICSI; Father-to-son sperm donation.

Introduction

Male factor is responsible in many cases waiting for in vitro fertilization (IVF) procedures. As Edwards and Brody note, male infertility is known as the main single cause of human infertility [1]. It is estimated to be responsible for almost 30% of the cases of primary infertility, 20% of secondary infertility and 20% of primary infertility involving both partners [1]. In severe cases of azoospermia, where no spermatozoa are found in ejaculated semen, microsurgically retrieved epididymal spermatozoa (MESA) and testicular sperm extraction (TESE), combined with intracytoplasmic sperm injection (ICSI), are reliable alternative solutions [2-9]. However, in cases of non-obstructive azoospermia where no spermatozoa can be found after a surgical intervention, sperm donation is the only alternative solution.

Sperm donation raises ethical and existential dilemmas, which are difficult to overcome especially by males [10-15]. Faced with these dilemmas, some couples prefer to use father-to-son sperm donation, in order to maintain some genetic lineage [12, 16].

This report describes three cases of non-obstructive azoospermia, where ICSI were obtained, by using fresh sperm donated from fathers-to-sons.

Case reports

Case 1

A young couple came to our center, after five years of unsuccessful attempts to conceive, due to male factor infertility. The husband was 28 years old. He suffered from varicocele, operated four years ago. In the previous three years, on the basis of repeated spermiograms, he was evaluated as asthenoteratozoospermic, kryptozoospermic (with less than 100,000 sperma-

tozoa per sample), or azoospermic. Three spermiograms in our center revealed total azoospermia. His biochemical examinations and the hormone profile were normal, as well as the semen culture was negative. The wife was 25 years old with no problems of infertility. Her hormone profile was normal.

They were counseled for sperm donation, but they insisted for an ICSI cycle, having the hope that even few spermatozoa could be found after TESE. From the very first moment, they were absolutely negative in heterologous insemination.

TESE was performed without finding even immature forms of spermatozoa. After this negative result, the couple was counseled again for sperm donation. They refused donation from anonymous donor and they suggested in turn, sperm donation from the father of the husband. The husband's father aged 65, accepted to donate his sperm. He underwent all appropriate examinations including HIV, Hepatitis B, Hepatitis C and spermiogram. His semen was suitable for ICSI (volume: 1.5 cc, concentration: 70 million spermatozoa/ml, motility 40%, 10% morphologically normal).

Ovarian stimulation was done due to the long protocol [17]. In brief, pituitary suppression was achieved with the GnRH agonist triptorelin (Arvekap depot 3.75 mg, Ipsen Pharma Biotech, France) and ovarian hyperstimulation with recombinant follicle stimulating hormone (recFSH) (Gonal-F®, Serono International S.A., Geneva, Switzerland) and purified urinary FSH (Altermon, Faran SACI, Athens, Greece). Ovulation was induced by injection of 10,000 IU human chorionic gonadotropin (hCG). Oocyte retrieval was performed 36 hours following hCG injection resulting in 12 oocytes of good quality. Eight oocytes were successfully fertilized by ICSI. Four embryos were transferred to the son's wife. She conceived and delivered three healthy children.

Case 2

Another couple came to our center after many years of attempts and four unsuccessful ICSI cycles. The husband was aged 38, suffered from kryptozoospermia due to varicocele. The varicocele was operated six years ago. The semen parameters did not show any improvement after the operation. The semen analysis in our center revealed total azoospermia. The biochemical

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examinations and the hormone profile were normal. The wife was 37 years old and suffered from polycystic ovarian syndrome. She had a poor response to the previous four ICSI cycles. The couple was counseled for sperm donation. They refused and insisted on another ICSI cycle, combining with TESE.

TESE was performed on the husband, with totally negative results. They were counseled again for sperm donation from an anonymous donor, but they emphatically refused. After that, they asked the husband's father, who was 77 years old, to donate his semen. He accepted and underwent all usual screening tests. His spermiogram was quite good (2 cc of semen, 40 million spermatozoa/ml, 5% morphologically normal, 30% motility). The wife followed a short stimulation protocol. Triptorelin 0.1 mg (Arvekap, Ipsen Pharma Biotech, France) was administered daily from the third day of the cycle and purified urinary FSH (Altermon, Faran SACI, Athens, Greece) from the sixth day. Ovulation was induced by injection of 10,000 IU hCG and oocyte retrieval was performed 36 hours following the hCG injection. She had a good response, resulting in eight oocytes. Seven oocytes were successfully inseminated and four embryos were transferred. There was a biochemical pregnancy.

Case 3

The third couple had undergone four years of unsuccessful attempts at natural conception. The wife was 30 years old and healthy. The husband was 37 years old and his spermiogram revealed azoospermia. TESE was performed with totally negative results. The couple was counseled about sperm donation. As the previous two couples, they refused and stated that they preferred to stop the attempts at assisted conception. A year later, they returned to the IVF center seeking an IVF cycle with the semen of the husband's father. During a discussion with the IVF director it was found that they had undergone a second TESE in another IVF center that also revealed non-obstructive azoospermia, with no spermatozoa or spermatids found in the testicular tissue. As in the previous cases, they were counseled to avoid father-to-son sperm donation based on two reasons: the complicated relationships of the offspring with them and the husband's father, as well as the potential medical risks of using a semen sample from a man of advanced age. They insisted on their decision and suggested screening the husband's father. The husband's father was 65 years old and consented to donate his semen. His medical history did not reveal any genetic disease. The screening tests were negative. His spermiogram was normal (3 cc, 80 million/ml, 15% morphologically normal, 55% motility). Although they were informed that the normality of the spermiogram did not exclude the existence of other abnormalities, such as chromosomal ones, the couple insisted on having an IVF cycle with the semen from the husband's father.

The wife followed a GnRH antagonist multiple dose protocol [18, 19]. Pituitary suppression was done with 0.25 mg/day of the GnRH-antagonist cetrorelix (Cetrotide, Serono International S.A., Geneva, Switzerland) from day 6 onwards until ovulation induction. Stimulation was achieved with recFSH (Gonal-F, Serono International S.A., Geneva, Switzerland). Ovulation was induced by administration of 10,000 IU hCG and oocyte retrieval was carried out 36 hours later. Six mature oocytes were retrieved; four of them were fertilized by ICSI and were transferred on day 2, resulting in a biochemical pregnancy.

Discussion

Sperm donation is a common practice in treatment of male infertility. In Greece, although there is a lack of official data, cryopreserved sperm from private sperm banks

is used in IVF practice. However, it is true that sperm donation is associated with great psychological implications for the couple [10-15]. From the male point of view, in sperm donation, there is a complete separation between biological and social filiation, while in oocyte donation this separation is only partial [13]. From the female point of view, in sperm donation there is not such a dramatic separation, as the genetic dissociation is partial and the pregnancy contributes to maintaining a strong biological bond between mother and child [13]. Faced with these problems, some couples do not consent receiving sperm donations. Others, as an alternative, prefer father-to-son sperm donation. It appears that those couples believe that father-to-son donations do not seem to be able not to solve, but do tone down these problems.

In the cases presented here, the three couples accepted sperm donation only after the very last hope of finding spermatozoa in the husband's testes had vanished. They completely refused a sperm donation from anonymous donors, despite the center's counseling. They also did not consent to sperm donation from a young relative, but they clearly preferred the husbands' fathers, even though they were elderly men and there was a lot of risk for the semen quality. It is worth noting that the three donors were healthy, they had satisfactory semen quality and ICSI secured the use of morphologically normal spermatozoa for fertilization. However, it is true that morphologically normal spermatozoa are not always healthy, as a number of studies have shown that sperm aneuploidy increases with age [20-22].

Cases with father-to-son sperm donation usually remain in the shadows. Secrecy is the key word for these cases, where couples as well as donors and other family members avoid any discussion of this issue. The three couples presented here did not easily discuss their thoughts and feelings on these issues even with the medical doctors and the psychologist of the IVF center. On the other hand, the available literature is extremely limited [12, 16]. Therefore, it is difficult to explain the choice of father-to-son sperm donation. It has been suggested that three reasons may explain the choice of husbands' fathers as donors [16].

First, there is the close genetic relationship between father and son that guarantees the maintenance of the genetic link. Second, there is the existence of strong emotional bonds between father and son. Third, the age of father. It seems that an old grandfather is difficult to take the role of "father" for the prospective offspring. Moreover, his life expectancy is limited, so the risk of claiming the role of "father" is negligible. The age is also crucial for diminishing the possibility of future negative father-daughter-in-law relations. Thus, with this type of donation, the future stability of the family seems to be secure [16]. On the other hand, the husbands' fathers seem to view sperm donation as a parental offer, as a gift, to their sons [12, 16].

Of course, there are also potential emotional risks to the offspring. As Marshall notes, the offspring's rearing father is its genetic brother and the rearing grandfather is its genetic father [12]. The impact of disclosing this

information to the offspring is unknown [12]. Secrecy is a central attitude not only in cases with father-to-son sperm donation but also in cases with heterologous gamete donation. Most recipient couples prefer to keep the way of conception secret, not only from the offspring but also from close friends and relatives [10, 11, 13-16, 23]. However, secrecy undoubtedly violates the offspring's right to know its origin, its way of conception and the medical history of its genetic father.

In Greece, there are no laws or official guidelines on intergenerational gamete donations and especially on sperm donation from father-to-son. As far as we know, there are no similar mentions in the laws or guidelines of other European Union countries or United States [24-26]. Furthermore, the available literature is very limited in this area. The lack of published studies on outcomes of father-to-son sperm donations, as well as the limited knowledge of the physicians involved in assisted reproduction methods on emerging ethical issues, makes difficult any discussion on the ethical implications, the counseling of couples and the decision making. The participation of a psychologist in every IVF team is unquestionably helpful [10, 12], but not always sufficient to solve the arising problems. However, it is essential, not only for psychologists, but also for physicians to spare adequate time in order to explore and discuss the emotional issues with the recipient couple and the donor, as well as to inform them about all medical risks.

The three cases presented here point out the ability of reproductive technologies to bring about novel alterations in the established family structures. The ethical and emotional issues that may arise are likely to be huge. We believe that it is urgent for the scientific community to exchange experience and opinions not only on the medical, but also on the ethical, emotional and social implications relating to intrafamilial gamete donation and particularly, father-to-son sperm donation.

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