

Successful Twin Pregnancy and Delivery Using Sperm that was Cryopreserved for 20 Years

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Abstract

Objective: To report a live birth following IVF treatment using sperm that was stored for nearly two decades.

Setting: PEDIEOS IVF center, Nicosia, Cyprus

Patient (s): 42-year-old former testicular cancer patient diagnosed with azoospermia and female partner age 31

Intervention(s): ICSI treatment using sperm sample that was cryopreserved with custom-made cryoprotectant and kept in storage for 20 years in rack and cane cryopreservation system. Resulting embryos cultured in a single continuous culture system to day 5. Two blastocysts were transferred into uterus of female partner

Main Outcome Measure(s): Successful twin pregnancy that resulted in two healthy live births

Conclusions: Sperm cryopreservation method before initiation of cancer therapy is an effective method for preserving male fertility. Proper care and maintenance of storage cylinders retains sample viability and fertilization ability post-thaw even after long term storage.

Keywords: Sperm Cryopreservation; Sperm Storage; ICSI; Cancer Treatment

Introduction

Improvements in cancer diagnostics and treatment protocols during the last decades led to an increased proportion of cancer patients reaching remission. Adolescent and childhood cancer can now be treated effectively with about 80% expected to be long-term survivors [1]. Although oncology treatment, such as chemotherapy and radiotherapy, have adverse effects on male fertility, resulting in permanent sterility in some cases. Cytotoxic drugs, such as nitrogen mustard derivatives and alkylating agents, can directly impair spermatogenesis while radiotherapy can induce permanent damage to germ cells. The cytotoxic effect of these treatments on the gonads is dependent on the type of protocol used e.g. combination of drugs as well as on the dose and duration of treatment.

An important concern about chemo and radiotherapy is the mutagenic effect that they have on germline. The ability of these treatments to induce mutations can be potentially associated with increased risk of congenital malformations, growth defects, and increased predisposition to cancer and juvenile diseases [2]. Although studies failed to show significant increased risks for children of male cancer survivors [2,3]. However it should be noted that children included in pregnancy outcome studies were conceived naturally without the use of assisted reproductive technologies. With the increasing use of ICSI procedure to achieve pregnancy, especially in cancer survivors with compromised gonadal function, there is a bypass of natural selection process that exists to eliminate genetically damaged spermatozoa [4]. Therefore, reproductive technologies might increase the risks for the offspring of previous cancer patients and reveal or exaggerate the effects of oncological treatment on reproductive outcome. More large scale studies are needed to address this issue.

Therefore, it can be concluded that sperm cryopreservation prior to cancer treatment is mandatory for maintaining a healthy reproductive potential. This case report describes a successful pregnancy and delivery using sperm that was cryopreserved for nearly 20 years.

We believe that these reports should continue to be published for validation of different procedures used and to promote this scientifically proven information to clinicians and patients.

Materials and Methods

(20% egg yolk, 15% glycerol in analar H₂O, Citrate and Glycine). The sperm sample was mixed in a drop-wise manner with equal volume of cryopreservation media and then aspirated in 0.5 mL straws. Straws were The patient sperm sample was cryopreserved on 3/1/1995 using custom made cryopreservation media kept in vapor phase for 30 minutes and then placed in liquid nitrogen for long-term storage. The sample was kept in MVE cylinders which have a rack and cane system for storage.

The sperm analysis before cryopreservation was performed manually using Makler chamber. In total 8 straws were cryopreserved from two different ejaculations.

IVF treatment

Following cancer treatment and remission the patient was diagnosed with azoospermia on 7/12/01. The sample came in handy when the patient decided to do IVF treatment in 2014. On 29/3/14 the sample was thawed in air for 15 minutes at room temperature and prepared for ICSI using double gradient centrifugation. The sample was used to inject 4 oocytes collected from the female partner the same day. After five days of culture two of the embryos reached the blastocyst stage. Both were transferred into the uterus using ultra-soft embryo transfer catheter.

Results

The sperm analysis before sperm cryopreservation was as follows; C = 10, 4×10^6 /mL, M=66% Grade a: 21%, b: 23%, c: 22% (C= concentration per mL, M= Motility (grades a, b-progressive motility, c non-progressive motility). The sample analysis after thawing was as follows; C = 5×10^6 /mL, M= 30% Grade a: 10%, b: 12, c: 8%. In total 4 MII oocytes were injected resulting in 3 2PN zygotes. Two of the embryos reached blastocyst stage after five days of culture. Their quality was 5AB and 2AB (where numbers (1 - 6) indicate degree of blastocyst expansion with 5 being the hatching blastocyst stage) and letters A-C/A-C indicate ICM and TE grade respectively (Gardner grading system). The level of bhCG hormone ten days after embryo transfer was 160 mIU/mL indicating the establishment of pregnancy. On 6th week of gestation two heart beats were detected on ultrasound. The pregnancy resulted in the delivery of two boys after 37 weeks of gestation. They were delivered with C-section and weighted 1681g and 2278g.

Discussion

This case report demonstrates that motility and function of cryopreserved sperm can be preserved for a long time. Although, we notice a 55% decrease in the motility of the sample after thawing, indicating that sperm cell integrity can be disrupted by the freezing-thawing procedure. We believe that extended period of storage can negatively influence sample integrity if the cryopreservation system is not properly maintained.

achieved using samples stored for 20 years [5], 21 years [6] and 28 years [7]. We believe that these studies should continue to be published in scientific journals for validation of protocols used and comparison of storage methods/conditions e.g. vials vs straws, rack and cane system vs carousel canister system etc. These data could ultimately enhance our knowledge about the optimal methodology for sperm storage. We strongly believe We acknowledge similar results from previous reports where successful pregnancies and live births were that these cases should also receive media attention as this would be the most effective way to promote the importance of sperm banking prior to cancer therapy.

Recent findings suggest that in some cases the cryopreserved sperm prior to oncological treatment may be preferable for establishing a pregnancy over the naturally produced sperm in the period following cancer therapy and remission. It was found that after chemotherapy for testicular cancer, chromosomal aneuploidies occur in sperm even after two years following treatment [8]. In sarcoma and Wilms's tumor treatment, chromosomal damage can persist from 5 to 18 years after completion of therapy [9]. These data highlight the importance of sperm banking in these cases. It remains to be established whether these sperm DNA alterations are associated with birth defects or other abnormalities to the fetus. Large follow up studies are needed to address this issue.

Recent statistics suggest that awareness also remains to be raised in female cancer patients. It is a pity referring to recent statistics of a UK Breast Cancer charity which estimates that around 5,000 young breast cancer patients are not offered fertility care/consultation before initiation of cancer treatment [10].

Conclusion

This emphasizes that the risks of damage to ovaries and hormonal disturbances that can possibly bring early menopause should be discussed with all women at the time of cancer diagnosis. To achieve this we believe that a fertility referral system in any health care organization will be most efficient to bring the best medical practice.

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