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CASE REPORT

Live birth after single embryo transfer of autologous cryopreserved oocytes from a patient with myelodysplastic syndrome who underwent allogenic peripheral blood stem cell transplantation

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We report a live birth after single embryo transfer derived from autologous cryopreserved oocytes of a patient with myelodysplastic syndrome who had undergone allogenic peripheral blood stem cell transplantation (PBSCT). In 2006, a 24-year-old female diagnosed with myelodysplastic syndrome was referred for fertility preservation before she underwent PBSCT. After controlled ovarian stimulation, 38 oocytes were retrieved for cryopreservation using a slow-freezing protocol. She was cured by PBSCT and entered menopause. After seven years, she requested thawing of the oocytes. She was prepared for a thawing cycle using hormone replacement therapy. Twenty-two cryopreserved oocytes were thawed, and 20 (91%) oocytes survived. Thirteen mature oocytes were inseminated by intracytoplasmic sperm injection. Ten (77%) oocytes were normally fertilized and 6 (60%) oocytes developed into blastocysts. Embryo transfer to her own uterus with one blastocyst was performed. Five blastocysts were vitrified. A sonographic exam at 7 weeks of gestation revealed one gestational sac with positive cardiac motion. A normal female baby weighing 2704 g was delivered at 40 weeks of gestation. A successful pregnancy from autologous cryopreserved oocytes is encouraging for cancer patients undergoing fertility preservation. For infertile cancer patients after PBSCT, we suggest the transfer of one embryo to reduce the risk of multiple pregnancies.

Conflicts of interest: The authors have no conflicts of interest relevant to this article.

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Introduction

Advancements in cancer therapies, particularly chemotherapeutics, have greatly improved the survival of cancer patients.[1] These treatments potentially damage their future reproductive function and fertility after cancer therapy.[2] Therefore, improvements in cancer treatments have led to a growing cohort of cancer survivors who experience premature gonadal failure and infertility. Therefore, the need for fertility preservation in cancer patients has increased in recent years.[3] Currently available strategies of fertility preservation in females include cryopreservation of embryos, oocytes, and ovarian tissue.

To date, >13 live births have been reported using ovarian tissue cryopreservation.[4] However, there is the potential risk that frozen-thawed ovarian tissue may contain cancer cells and reintroduce the disease after grafting, particularly hematological cancer diseases. In cases of leukemia, malignant cells have been detected in the cryopreserved ovarian tissues.[5] Embryo and oocyte cryopreservation have no risk of reintroducing cancer cells. Embryo cryopreservation is feasible for married women, and oocyte cryopreservation is suitable for post-pubertal females without a committed male partner.[6,7]

Patients after chemotherapy and total body irradiation for bone marrow transplantation have an increased incidence of preterm birth at pregnancy.[8] In 2002, we initiated an oocyte cryopreservation program for female cancer patients. A total of 35 cancer patients achieved oocyte cryopreservation. However, only one patient requested warming of her oocytes. We present a case report of a live birth after single embryo transfer (SET) of autologous cryopreserved oocytes from a patient with myelodysplastic syndrome who had undergone allogenic peripheral blood stem cell transplantation (PBSCT).

Case report

In 2006, a 24-year-old unmarried female diagnosed with myelodysplastic syndrome was referred to our institute for fertility preservation. She had symptoms of dizziness, palpitations, and severe anemia. At that time, every 2—3 months, she needed to receive a blood transfusion. The medical oncologist performed human leukocyte-associated antigen (HLA) tests for her and her siblings. The results revealed that the HLA antigens of her elder sister were compatible with her. Peripheral blood stem cell transplantation was planned for her; the stem cells came from her elder sister. Before the PBSCT, the doctor referred her to our institute for fertility preservation. Our gynecologist counseled her concerning oocyte cryopreservation. She then decided on this procedure for preserving gametes prior to undergoing PBSCT. This study was approved by the Ethic Committee of National Taiwan University Hospital (Taipei, Taiwan). Informed consent was obtained from the patient.

The patient had regular menstrual cycles. Her baseline levels of follicle-stimulating hormone (FSH), luteinizing hormone (LH), and estradiol (E2) levels were 5.1 mIU/mL, 5.3 mIU/mL, and 31 pg/mL, respectively. An ultrasonographic examination revealed a normal uterus and normal ovaries. The patient was treated with a short gonadotropin-releasing hormone agonist (GnRHa) protocol. Buserelin nasal spray (Supremon; Hoechst, Frankfurt am Main, Germany) at a dosage of 200 μg four times daily was started on Day 2 of the menstrual cycle, and recombinant FSH (Gonal-f; Serono, Frankfurt, Germany) at 225 IU daily subcutaneously was started on Day 5. Ovarian responses were monitored with serial transvaginal ultrasonography exams and serum E2, LH, progesterone measurements. When the two leading follicles were over 18 mm in diameter, final maturation was triggered with 10,000 IU of human chorionic gonadotropin (hCG) (Profasi; Serono). Transvaginal oocyte retrieval was performed at 35 hours after hCG injection.

Thirty-eight cumulus-oocyte-complexes were retrieved and cumulus cells were removed for cryopreservation. We used a slow-freezing protocol to freeze 38 oocytes, which included 26 mature oocytes and 12 immature oocytes.[9,10] In 2007, she underwent PBSCT after pretreatment with chemotherapy. She was regularly followed up by her medical oncologist and was free of disease. However, she became entirely amenorrheic, and the hormonal examinations revealed hypergonadotropic hypogonadism. She received hormonal replacement therapy for premature menopause.

In 2011, she was married. She had regularly used hormone replacement therapy, which consisted of estradiol valerate (Estrade; Synmosa, Taipei, Taiwan) at 4 mg/day for 25 days plus 10 mg/day of medroxyprogesterone acetate (Provera; Pfizer, Caguas, Puerto Rico) for 14 days. Transvaginal sonography revealed a normal uterine size (6.2 cm × 3.9 cm × 2.8 cm), but relatively small ovaries (1.9 cm × 0.7 cm × 0.6 cm and 1.2 cm × 0.7 cm × 0.5 cm). In 2013, at the age of 31 years, she visited our institute and requested the thawing of her oocytes.

For the thawing cycles, endometrial preparation involved a hormonal replacement cycle because of her menopausal status. The protocol of hormonal replacement cycle has been previously described,[10] We prepared the endometrium for the patient from Day 3 of the menstrual cycle by prescribing oral estradiol valerate (2 mg) with incremental dosages of 4 mg from Days 3—8; 8 mg from Days 9—11; and then 12 mg on Day 12. On Day 14, the serum E2, LH, and progesterone levels were 540 pg/mL, 88 mIU/mL, and 0.2 ng/mL, respectively.

An ultrasonographic examination revealed an endometrial thickness of 12 mm. We added intravaginal progesterone gel of Crinone (Crinone 8%; Fleet Laboratories, Watford, UK) at 90 mg daily for 2 days from Day 14 onward and Crinone (Fleet Laboratories) at 90 mg twice daily from Day 16 onward.

Twenty-two cryopreserved oocytes were thawed on Day 14. For thawing, the straws were removed from the liquid nitrogen, maintained at room temperature for 30 seconds, and then put into a 30°C water bath for 40 seconds. The cryoprotectants were removed by stepwise dilutions.[9,10] The oocytes were finally transferred to a culture medium and cultured for 3 hours at 37°C in an incubator with 5% carbon dioxide atmosphere.[10] Twenty (91%) oocytes survived, and 13 mature oocytes were inseminated by intracytoplasmic sperm injection. The other seven oocytes were immature and were not used. Ten (77%) oocytes were normally fertilized and 6 (60%) oocytes developed into blastocysts. Single embryo transfer with one blastocyst to