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Taiwanese Journal of Obstetrics & Gynecology 51 (2012) 651–653

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Research Letter

Oocyte vitrification in a single woman with diminished ovarian reserve resulting in live birth

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Accepted 5 January 2012

Fertility preservation is crucial for women experiencing diminished ovarian reserve (DOR) due to disease treatments or aging. From preserving ovarian tissues to oocytes, scientists are trying to find more convenient, cost-effective ways to meet women's fertility needs. Since the first successful live birth from a human frozen/thawed oocyte in 1986 [1], more researchers have devoted themselves to this field, developing techniques and applications for oocyte cryopreservation. Progress in human oocyte cryopreservation, especially vitrification along with its obstetric outcome, has been one of the major issues in reproductive medicine recently. Chen et al [2] reported a 75% survival rate, 67% fertilization rate, and 33% pregnancy rate following a new oocyte slow freezing/thawing procedure. Vitrification is thought to be a highly efficient technique for embryo and oocyte cryopreservation [3–5]. The vitrification of oocytes allows higher postwarm survival rates than slow freezing. However, significant improvements have been achieved in both cryopreservation methods [2,6].

Several research studies on the outcome of oocyte cryopreservation have been published. Kim et al [7] reported that in fertile women, vitrification of oocytes produces pregnancy and implantation rates comparable to those of frozen embryos. Although the data were limited, a systematic review of cryopreserved oocytes showed no obvious association with adverse pregnancy outcome [8]. A multicenter, prospective clinical trial to evaluate the efficacy, safety, and outcome of human oocyte cryopreservation is currently ongoing [9]. However, there is still a need for more supportive evidence of oocyte vitrification.

Studies in this field have mainly focused on young or fertile women needing cryopreservation for medication purposes [7,10–14], but rarely has there been concern about women who are at an advanced maternal age or infertile [15,16]. Because oocyte number and quality begin to decline from age 35 years onward, it is necessary to evaluate the possibility of "self-cryobanking" for women with DOR who could then conceive using their own donor eggs. From the oocyte banking point of view, the greater the number of oocytes collected, the better the chances of ensuring offspring. Therefore, we have proposed a strategy whereby we perform multiple oocyte retrieval–vitrification cycles to accumulate a sufficient number of oocytes for such patients.

A 39-year-old single woman came to our clinic in March 2009 asking for fertility preservation. Despite poor ovarian function, she did not want to give up her chance of becoming pregnant with her own biological child. After a detailed consultation on the treatment process and under a full consent agreement, she decided to vitrify her oocytes.

In April 2009, a serologic examination of her hormone profile and a transvaginal ultrasound were done on Day 2 of her spontaneous menstrual cycle. The hormone profile was as follows: antimüllerian hormone, 0.77 ng/mL; follicle-stimulating hormone, 22.1 mIU/mL; luteinizing hormone, 2.67 mIU/mL; estrogen, 38.1 pg/mL; progesterone, 0.97 ng/mL. Four antral follicles were observed. Prior to ovulation stimulation, one shot of gonadotropin-releasing hormone agonist (Decapeptyl, Ferring Pharmaceuticals, Taiwan) per day was administered on Day 2 for 4 days in addition to a recombinant human growth hormone (Saizen, Merck Serono, Taiwan) on Day 3 for 3 days to induce endogenous hormone release. Ovulation stimulation started on Day 5 by daily injection of menotropin (Menopur, Ferring Pharmaceuticals, Taiwan) 225 IU for 2 days followed by 75 IU until the day of ovulation triggering. As one follicle reached the diameter of 1.7 mm, human chorionic gonadotropin (hCG) was injected. Transvaginal ultrasound-guided oocyte retrieval was performed approximately 34–35 hours after the hCG trigger. One oocyte cumulus corona complex was obtained and placed in hyaluronidase 80 mIU/mL for 10–15 seconds. The oocyte was then transferred to regular tissue culture media for complete removal of the corona cells within 3 hours by repeated aspiration with a finely pulled

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http://dx.doi.org/10.1016/j.tjog.2012.09.025

pipette. One matured (metaphase II) oocyte was vitrified 1 hour later by the Cryotop method (Kitazato Bio-Pharmaceuticals, Japan).

The second oocyte retrieval was performed in the following cycle by initiating ovulation stimulation on Day 6 with clomiphene citrate 100 mg/day for 6 days then with menotropin 150 IU/day on Day 13 until Day 17, the day of the hCG trigger. Approximately 34–35 hours after that, a transvaginal ultrasound-guided oocyte retrieval was performed. One oocyte was harvested and treated within 3 hours after oocyte retrieval. One matured oocyte was vitrified 1 hour later using the Cryotop method.

In November 2009, the woman married and wanted to undergo a natural fresh in vitro fertilization (IVF) cycle. No oocyte was obtained this time, so she requested a warmed oocyte-IVF cycle. Two previously gathered vitrified oocytes were warmed and both survived. Fertilization was achieved via intracytoplasmic sperm injection with a fresh semen sample 2 hours postwarming, and after 16–18 hours, two pronuclei were observed in both zygotes. The zygotes were then transferred to global media (LifeGlobal, Guilford, CT, USA) supplemented on Day 1 with 10% Quinns Advantage serum protein substitute (CooperSurgical, Inc., Trumbull, CT, USA).

Prior to the embryo transfer, the patient underwent a cervical bacteria culture, chlamydia and human papillomavirus screening tests, and hysteroscopy to evaluate the uterine cavity. The bacterial and viral tests were negative. The hysteroscopy revealed negative abnormal findings in the uterine cavity with bilateral tubal ostium opening. The endometrial lining was 8 mm on Day 12 of the cycle, the day of the oocyte warming. Endometrium preparation began on the same day with oral progesterone 300 mg/day. Three days later, two eight-cell embryos were transferred back to the patient's womb under transabdominal ultrasound monitoring. We achieved luteal supplementation through vaginal progesterone 180 mg combined with oral estradiol 5 mg daily. Her Day 7 serum progesterone level was 15.8 ng/mL.

The patient's serum β-hCG levels were noted at 373.07 mIU/mL and 1762.73 mIU/mL, respectively, on Days 16 and 19 after the embryo transfer. Transabdominal ultrasound showed one viable singleton intrauterine pregnancy at 7 weeks' gestation. During her pregnancy, she developed pregnancy-induced hypertension; however, the situation was well controlled. A healthy baby girl weighing 2720 g was delivered by cesarean section after 39 weeks, 2 days' gestation. At the follow-up at 9 months the baby was developing normally.

This study documents a healthy live birth after oocyte vitrification. We also demonstrated that fertility could be reserved in women with DOR through multiple oocyte retrieval–vitrification cycles. This strategy could be applied not only in women who would like to preserve their fertility, but also in those who plan to undergo IVF treatment. For a woman with DOR who is older than 43 years, the pregnancy and live birth rates might be reduced due to fewer oocytes/embryos being transferred per IVF-embryo transfer (ET) cycle. We proposed dividing a traditional IVF-ET treatment into two parts. Multiple oocyte retrieval-vitrification cycles to accumulate oocytes would be performed first. Once a sufficient number of oocytes is reached (depending on the woman's age), the second part, warming and the following IVF-ET procedure, would be completed.

In women treated with warming oocyte-ET, an inverse correlation is found between the ongoing pregnancy rate and an age older than 40 years. The cumulative ongoing pregnancy rate was found to be highest when the woman is 34 years of age or younger [17]. According to the prospective controlled study of Kim et al [7], in young and fertile women who underwent IVF cycles, a high pregnancy rate and live birth rate was maintained after 6 months of oocyte vitrification. This result hinted that if single women of reproductive age could preserve their oocytes as early as possible, they could then determine for themselves in the future when they are ready for marriage and childbearing without compromising the pregnancy rate.

The clinical outcome in our report suggests that the age limitation could be overcome by storing vitrified oocytes, thus making life planning more flexible. The request for fertility preservation could be viewed as preventive medicine for infertility and extended to nononcologic applications. The proposed oocyte "self-cryobanking" could benefit women of reproductive age by preserving their reproductive potential. As time passes, this concept is becoming more popular and gradually more acceptable.

References

[1] Chen C. Pregnancy after human oocyte cryopreservation. Lancet 1986;1:884–6.
[2] Chen SU, Lien YR, Chen HF, Chang LJ, Tsai YY, Yang YS. Observational clinical follow-up of oocyte cryopreservation using a slow-freezing method with 1,2-propanediol plus sucrose followed by ICSI. Hum Reprod 2005;20:1975–80.
[3] Paffoni A, Guarneri C, Ferrari S, Restelli L, Nicolosi AE, Scarduelli C, et al. Effects of two vitrification protocols on the developmental potential of human mature oocytes. Reprod Biomed Online 2011;22:292–8.
[4] Kuwayama M. Highly efficient vitrification for cryopreservation of human oocytes and embryos: the Cryotop method. Theriogenology 2007;67:73–80.
[5] Kuwayama M, Vajta G, Kato O, Leibo SP. Highly efficient vitrification method for cryopreservation of human oocytes. Reprod Biomed Online 2005;11:300–8.
[6] Chen SU, Yang YS. Slow freezing or vitrification of oocytes: their effects on survival and meiotic spindles and the time schedule for clinical practice. Taiwanese J Obstet Gynecol 2009;48:15–22.
[7] Kim TJ, Laufer LR, Hong SW. Vitrification of oocytes produces high pregnancy rates when carried out in fertile women. Fertil Steril 2010;93:467–74.
[8] Wennerholm U-B, Söderström-Anttila V, Bergh C, Aittomäki K, Hazekamp J, Nygren KG, et al. Children born after cryopreservation of embryos or oocytes: a systematic review of outcome data. Hum Reprod 2009;24:2158–72.
[9] Ezcurra D, Rangnow J, Craig M, Schertz J. The Human Oocyte Preservation Experience (HOPE): a phase IV, prospective, multicenter, observational oocyte cryopreservation registry. Reprod Biol Endocrinol 2009;7:53.

[10] Kim TJ, Hong SW. Successful live birth from vitrified oocytes after 5 years of cryopreservation. J Assist Reprod Genet 2011;28:73–6.
[11] Yang D, Brown SE, Nguyen K, Reddy V, Brubaker C, Winslow KL. Live birth after the transfer of human embryos developed from cryopreserved oocytes harvested before cancer treatment. Fertil Steril 2007;87:1469.e1–4.
[12] Cobo A, Domingo J, Pérez S, Crespo J, Remohí J, Pellicer A. Vitrification: an effective new approach to oocyte banking and preserving fertility in cancer patients. Clin Transl Oncol 2008;10:268–73.
[13] Rienzi L, Romano S, Albricci L, Maggiulli R, Capalbo A, Baroni E, et al. Embryo development of fresh 'versus' vitrified metaphase II oocytes after ICSI: a prospective randomized sibling-oocyte study. Hum Reprod 2010;25:66–73.
[14] Del Mastro L, Giraudi S, Levaggi A, Pronzato P. Medical approaches to preservation of fertility in female cancer patients. Expert Opin Pharmacother 2011;12:387–96.
[15] Parmegiani L, Cognigni GE, Bernardi S, Ciampaglia W, Pocognoli P, Filicori M. Birth of a baby conceived from frozen oocytes of a 40-year-old woman. Reprod Biomed Online 2009;18:795–8.
[16] Knopman JM, Noyes N, Grifo JA. Cryopreserved oocytes can serve as the treatment for secondary infertility: a novel model for egg donation. Fertil Steril 2010;93:2413.e7–9.
[17] Ubaldi F, Anniballo R, Romano S, Baroni E, Albricci L, Colamaria S, et al. Cumulative ongoing pregnancy rate achieved with oocyte vitrification and cleavage stage transfer without embryo selection in a standard infertility program. Hum Reprod 2010;25:1199–205.