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CASE REPORT

Case Report: Successful delivery in a 44-year-old woman using vitrified human oocytes taken from the woman at 41 years of age [version 1; peer review: 1 approved with reservations, 2 not approved]

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Abstract

Successful pregnancies and deliveries are rare in women over 40 years of age. To date, no case report has been published about a successful delivery in a woman over 40 years of age using vitrified oocytes obtained through social egg freezing from a woman over 40 years of age. Here we report a case of a successful live birth from a 44-year-old woman using vitrified oocytes taken from the woman at 41 years of age; the patient used the technique for social reasons. The 44-year-old patient delivered a 2534 g female infant by Caesarean section in the 37th week of pregnancy. The female infant's Apgar scores were 9 at 1 min and 9 at 5 min. The female infant exhibited no anomalies and is developing normally under the close surveillance of pediatricians.

However, the concept of social egg freezing has medical, ethical and social problems. Furthermore, the rate of live births differs among clinics and/or hospitals due to variations in the vitrification and warming techniques used. Therefore, information from individual clinics and/or hospitals about the risks, the rates of successful live births and the cost of social egg freezing should be provided to patients to aid in the patient's decision-making process.

Keywords

Women over 40 years old , vitrified human oocytes , social egg freezing , live birth

Open Peer Review

Approval Status

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10 May 2016	view	view	view

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Any reports and responses or comments on the article can be found at the end of the article.

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Introduction

Given the advancement in technology for human egg freezing, the use of social egg freezing is increasing in developed countries^{1,2}. The increase in social egg freezing is associated with a number of different personal, professional, economical and psychological reasons^{1,2}.

However, successful pregnancies and deliveries are rare in women over 40 years of age^{1,2}. Furthermore, no case report about a successful delivery from a woman over 40 years of age using vitrified oocytes obtained through social egg freezing from a woman over 40 years of age has been published to date (as assessed through a PubMed database search).

Case

The patient visited our *in vitro* fertilization (IVF) clinic in April 2012. The patient was a 41-year-old woman who wanted to freeze her eggs for social reasons. She provided written informed consent. From April 2012 to June 2013, 8 oocytes were vitrified through ultra-rapid cooling using a high concentration of cryoprotectants (15% ethylene glycol + 15% DMSO + 0.5 mol/l sucrose) in a cryo device (Vitrification Media Kit, KITAZATO CORPORATION, okyo, Japan) by plunging the oocytes into liquid nitrogen (-196°C). The 8 oocytes were cryopreserved within liquid nitrogen (-196°C). The vitrified oocytes were thawed at the time of use. In June 2014, two embryos (day 2; a vitrified oocyte-derived embryo and a standard-derived embryo) were transferred to the uterus. The embryo transfers were carried under ultrasound guidance when endometrium thickness reached 7.0 mm. However, the patient's pregnancy was not confirmed by the presence of a gestational sac (GS) at this time.

In August 2014, an embryo (day 5) from a vitrified oocyte was transferred to the uterus (the endometrium thickness: 7.5 mm), and the patient's pregnancy was confirmed by the presence of a GS at 5 weeks (Figure 1). Repeated ultrasonography during the pregnancy revealed normal fetal growth and development. The 44-year-old

patient delivered a 2534 g female infant by Caesarean section in the 37th week of pregnancy in May 2015. The female infant's Apgar scores were 9 at 1 min and 9 at 5 min. The female infant exhibited no anomalies and is developing normally under the close surveillance of pediatricians.

Discussion

Human oocyte vitrification holds great promise for women who need to preserve their fertility due to cancers that require chemotherapy or radiation^{1,2}. This technique is also referred to as "social egg freezing," and many women who wish to delay pregnancy and/or delivery to pursue educational or professional goals want to have this option available to them^{1,2}. However, the guidelines of the American Society for Reproductive Medicine (ASRM) caution against the use of oocyte vitrification to circumvent the effects of age on the reproductive potential of healthy women given that there are insufficient data to support the safety, efficacy, ethics, emotional risks and cost-effectiveness of oocyte cryopreservation³. In 2013, the Japan Society for Reproductive Medicine (JSRM) issued a guideline allowing egg freezing for women under 40⁴. In addition, in 2015, an expert panel from the Japan Society of Obstetrics and Gynecology (JSOG) said it is not recommended that young and healthy women preserve their frozen eggs for future pregnancies and deliveries^{4,5}.

Furthermore, after performing a PubMed database search, no case reports have been published demonstrating the safety and efficacy of oocyte cryopreservation in women over 40 years of age who used the technique for social reasons. Therefore, we report a case of a successful live birth from a 44-year-old woman using vitrified oocytes obtained through social egg freezing from the woman at 41 years of age. Although the oocyte-to-baby rate was 1.8% and the number of oocytes typically needed to achieve a baby in women over 40 years of age is 55.5⁶, we were fortunately able to obtain a successful example. However, the concept of social egg freezing has medical, ethical and social problems. In general, a woman's ovarian reserve declines as she ages, resulting in fewer oocytes and

Figure 1. The patient's pregnancy was confirmed by the presence of a gestational sac (GS) at 5 weeks.

an increased risk of embryonic aneuploidy¹. Although we do not necessarily recommend having a child in the later stages of life, many patients who visit our IVF clinic are older than 40 years of age. Therefore, careful counseling is required because the patients must understand the uncertainties regarding the safety and efficacy of social egg freezing.

In addition, the rates of live births differ among clinics and/or hospitals due to variations in the vitrification and warming techniques used¹. Therefore, information from individual clinics and/or hospitals about the risks, the rates of successful live births and the cost of social egg freezing should be provided to patients to aid in the patient's decision-making process.

Conclusion

We report a successful live birth from a 44-year-old woman using vitrified oocytes obtained through social egg freezing from the woman when she was 41 years old. However, the concept of social

egg freezing is controversial. Therefore, information concerning this process should be disclosed to aid in the patient's decision-making process.

Consent

Written informed consent for publication of the clinical details and clinical images was obtained from the patient.

Author contributions

All authors equally contributed to the writing of this manuscript.

Competing interests

No competing interests were disclosed.

Grant information

The author(s) declared that no grants were involved in supporting this work.

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Title is appropriate and indicates what the substance of the case report is.

Unfortunately, there are certain issues need to be addressed.

As expected, the likelihood of a successful pregnancy in a woman the age of 40 years and above would be low. Authors need to address the issue as to which individuals are likely to have a successful pregnancy.

Genetic, environmental and hormonal milieu and family history, age at menopause in other females in the family need to be addressed.

There is no case report in the literature - PubMed - as it is not impossible for women to have a successful pregnancy after the age of 40 yrs of age and hence not a rare event.

It would be worthwhile if authors were to analyse all these factors and genetic studies if possible to describe factors contributing to successful egg donation and pregnancy thereafter.

Lastly, why did this patient undergo caesarean delivery to deliver her baby? This is an unanswered question.

Competing Interests: No competing interests were disclosed.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to state that I do not consider it to be of an acceptable scientific standard, for reasons outlined above.

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In this manuscript the authors present a case report of social oocyte vitrification in a woman at age 41 that resulted in a live birth when the oocytes were warmed and fertilized 3 years later. This may be the first reported case of successful pregnancy from vitrified oocytes over age 40.

In my opinion, this case adds nothing new to the literature. There is no new technology nor surprising new findings since standard vitrification techniques and routine in vitro fertilization were used in this patient. The unusual finding is that she achieved a successful pregnancy.

In contrast, this case report may raise false hope for other women over age 40 who have delayed pregnancy and think that social egg freezing may be an option to preserve their fertility. As the authors themselves point out, the clinic that perfected vitrification of oocytes and that has the most experience with the technique, estimated that 55 oocytes would have to be vitrified in a woman over age 40 to achieve a pregnancy and live birth (Cobo et al, 2015). I believe that this number should be enough to discourage any woman from considering social or other oocyte freezing over age 40, or any clinic from offering this procedure to women over 40. In our clinic, we have an upper age limit for social age freezing of 39 years, although I am aware of other clinics in which this is not the case.

The patient in the present case report was lucky to have a euploid oocyte that survived, was fertilized and implanted allowing her to conceive. In the course of a year, from April 2012 to June 2013 she had 8 oocytes vitrified. Presumably it required several cycles to obtain the 8 oocytes and the authors should provide this information. The first embryo transfer in which the patient did not conceive included an embryo derived from one of the vitrified oocytes and one from a fresh IVF cycle, suggesting that the woman was still ovulating. The authors need to describe the endometrial preparation technique used for the successful embryo transfer. Was it an exogenous estrogen and progesterone hormonal preparation of the endometrium or a natural cycle? If the latter, how did the authors ensure that the pregnancy was not achieved as a result of natural conception of an ovulated oocyte?

Competing Interests: No competing interests were disclosed.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to state that I do not consider it to be of an acceptable scientific standard, for reasons outlined above.

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- *Title and Abstract:* The title is reflective of the content of the article. The abstract adequately summarizes the article.
- *Article content:* The topic of the case report is very interesting. The authors can expand the current body of knowledge on elective fertility preservation in this age group by providing more details about the patient. For instance demographic information such as the patient's gravity, parity, medical comorbidities, BMI, ovarian reserve (Day 3 FSH, E2, AMH, antral follicle count) are missing. It can be inferred that the patient underwent more than one stimulation cycle. The number of cycles she underwent to reach 8 oocytes and the protocol is also omitted. The grade of the embryos transferred was also not shared. Most importantly the indication for the early term c-section at 37 weeks and any maternal medical conditions that developed antenatal, intra-partum or post-partum are extremely relevant and should be reported. Providing more information would allow the information to be applied in similar scenarios.
- *Conclusions:* The conclusion was well thought out. However, given very little information was given about the patient is difficult to assess if alternative conclusions would be more plausible.

Competing Interests: No competing interests were disclosed.

We confirm that we have read this submission and believe that we have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however we have significant reservations, as outlined above.

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