Case Report

Live Birth from ICSI-TESA into *In Vitro* Matured Oocytes: A Case Report

Şafak Hatırnaz [1], Ebru Hatırnaz [1], Murat Bakacak [2*], Mehmet Sühha Bostancı [3], Melahat Atasever [4]

1- Clinart IVF Center, Trabzon, Turkey
2- Department of Obstetrics and Gynecology, Kahramanmaras Sutcu Imam University, School of Medicine, Kahramanmaraş, Turkey
3- Department of Obstetrics and Gynecology, Sakarya University Research and Education Hospital, Sakarya, Turkey
4- Department of Obstetrics and Gynecology, Giresun University, School of Medicine, Giresun, Turkey

* *Corresponding Author:* Murat Bakacak, Kahramanmaras Sutcu Imam Universitesi, Tıp Fakultesi, Avsar Kampusu, Merkez, Kahramanmaras, Turkey
E-mail: muratbakacak46@gmail.com

Received: Nov. 23, 2014
Accepted: Mar. 15, 2015

Abstract

Background: Repeated *in vitro* Fertilization (IVF) failure together with Ovarian Hyperstimulation Syndrome (OHSS) is one of the distressing situations leading couples to search for alternative treatment options. For such patients with Polycystic Ovarian Syndrome (PCOS) who have experienced Ovarian Hyperstimulation Syndrome, mild ovarian stimulation with *in vitro* oocyte maturation could be a promising alternative. Testicular Sperm Aspiration (TESA) of spermatozoa from a known obstructive azoospermic patient is a limiting factor for IVM (*in vitro* maturation) but the couple reported here accepted mild IVF -IVM with TESA.

Case Presentation: In the treatment of a 32-year old woman, 9 immature oocytes were retrieved, 5 *in vitro* matured oocytes (maturation rate 55%) and after fertilization by Intracytoplasmic Sperm Injection (ICSI), 3 oocytes (fertilization rate 60%) which had two pronuclei and two good quality embryos on day 2, were transferred. A live pregnancy was observed by ultrasound scan and healthy infant was delivered.

Conclusion: Although the number of births from ICSI of immature oocytes injected with surgically derived sperm is quite low, the selection of this mode of therapy as an alternative to conventional IVF will overcome the limitations and provides a new option in IVF practice.

Keywords: *In vitro* maturation, Oocytes, Pregnancy, Testicular sperm aspiration.
To cite this article: Hatırnaz Ş, Hatırnaz E, Bakacak M, Bostancı MS, Atasever M. Live Birth from ICSI-TESA into *In vitro* Matured Oocytes: A Case Report. J Reprod Infertil. 2015;16(4):236-238.

Introduction

In vitro oocyte maturation (IVM) with a mild IVF program is a well-known laboratory procedure, which has been used in Assisted Reproductive Technologies (ARTs) cycles as an alternative to conventional IVF. Although the clinical applications have been limited to cases of PCOS who have experienced OHSS, it can also be used in normal ovarian reserve patients and in patients who have failed to conceive by conventional ART treatments. Since IVM needs only mild or no ovarian stimulation, there is no risk of OHSS. Despite no contraindications, there are hesitations about using IVM in cases with surgical sperm retrieval and selecting TESA-IVM in couples with obstructive azoospermia, but it is an effective treatment option which can result in successful pregnancies and live births (1, 2). Since IVM has a limited use in ART practice, convincing couples with male factor infertility such as azoospermia for IVM is very difficult. However, the risk of OHSS and failed IVF attemps makes the decision for IVM much easier in such couples. The number of cases of IVM in azoospermia is limited in the literature and only limited centers have experience on IVM in azoospermia, thus increasing the number of studies in such cases may encourage IVF centers to use this modality in their ruotine practice.

Case Presentation

A 32 year old woman and her 37 year old husband presented at Clinart IVF Center (Trabzon,

Turkey) in 2011 with a 7-year history of primary infertility with two failed attempts at TESA-ICSI. Ultrasound examination on day 3 of the menstrual cycle revealed the existance of bilateral polycystic ovaries. The male was diagnosed with obstructive azoospermia and had undergone surgery for TESA for each ICSI attempt. Many treatment options were discusssed with the couple together with IVM-TESA but due to a history of OHSS in one of the previous attempts, the couple decided to be treated with this treatment modality. There was no history of other medical or surgical diseases and hormonal parameters were as expected (FSH 6.28 *mIU/ml*, LH 7.73 *mIU/ml*, PRL 42.96 *ng/ml* and TSH 2.68 *mIU/ml*). In their first conventional ICSI attempt, 26 oocytes were collected, 3 embryos were transferred and following OHSS, she had negative β hCG value. In their second attempt at the same center, 11 oocytes were recovered and only 1 embryo was transferred and resulted in failure. The semen analysis revealed no sperm. The hormone parameters of the male supported the previous diagnosis of obstructive azoospermia (FSH 5.81 *mIU/ml*, LH 5.97 *mIU/ml*, TSH 2.62 *mIU/ml* and PRL 13.50 *ng/ml*).

The female started a semi IVF-IVM program on day 3 and was given 3 days of 75 *IU* recombinant FSH (Gonal-F, Merck Serono, Switzerland) Sc for FSH priming together with estrogen support for endometrial thickening. The patient was evaluated on day 6 and on day 8, repetitively for endometrial triple line pattern and when endometrial thickness of 8 *mm* was achieved together with follicles less than 12 *mm*, 250 microgram Human Chorionic Gonadotropin Alpha (Ovitrelle, Merck Serono, Switzerland) was administered subcutaneously for triggering. After 36 *hr*, 9 immature oocytes were collected and testicular sperm were derived by TESA at the same day of OPU under general anesthesia. After filtration and 26 *hr* after the incubation in IVM culture medium (Origio medicult IVM medium, Denmark), the oocytes were detached (denuded) from the cumulus cell mass and 5 matured oocytes (55% maturation rate) were injected with TESA derived fresh sperm and 3 oocytes with 2 pronuclei (60% fertilization rate) were generated. On the second day, 2 embryos with grade 2 morphology were transferred. IVM laboratory course is depicted in figure 1. A successful pregnancy was achieved. First fetal cardiac activity was determined on abdominal ultrasound at 6 weeks and 6 days and the patient had a safe cesarean-section delivery of a healthy male infant (birthweight 4000 *g*) at 38 weeks of gestation.

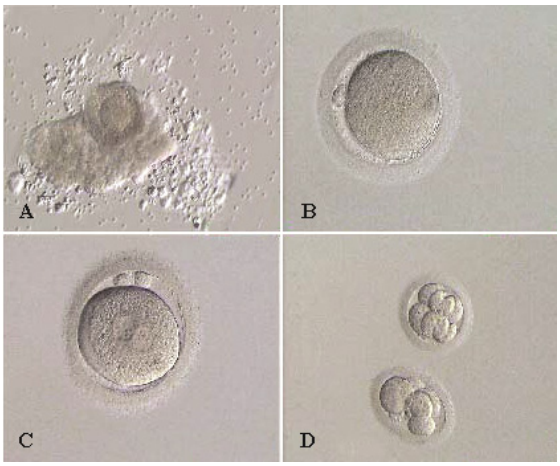

Figure 1. IVM laboratory course; A: Obtained GV oocyte with cumulus corona complex; B: MII oocyte following IVM; C: PN stage; D: Transferred embryo

Discussion

Immature oocyte collection in a mild IVF program is still controversial for many IVF specialists and the impact of IVM is decreased compared to conventional methods. However, after the failure of conventional attempts, the low costs, no OHSS risk and possibility of being repeated in a short time make IVM a tempting prospect for couples (1). The most important point in IVM is the optimized culture media since immature oocytes have immature cumulus cells that may lead to diminished nutritional support for oocytes *in vitro* (2). The IVM culture medium is supported by the maternal serum albumin (3). As it conforms with healthcare regulations, IVM has been widely used in Italy. The study of Fadini et al. by TESE of NOA with IVM and 20 normoovulatory and one PCOS patients who underwent 27 IVM cycles. The results of TESE on Non Obstructive Azoospermia (NOA) were compared with conventional ICSI in terms of respective pregnancy and fertilization rates and it was concluded that IVM may represent an option in NOA cases (4). In another study by Son et al., TESE-IVM cases were compared with IVM with ejaculated sperm and 21 patients through 24 cycles were evaluated. Clinical pregnancies were 37.5% of cases and it was concluded that IVM combined with TESE-ICSI could be a suitable option for couples with PCO and azoospermia (5). The introduction of ICSI for ART treatment has offered azoospermic patients the possibility of pregnancy following

surgical sperm removal (6). The first live birth from TESE-IVM was reported by Ahmad Kamal et al. in 2001 at McGill University, Canada (7). At a recent meta-analysis, the authors showed decreased live birth and implantation rates in comparison to conventional IVF/ICSI for patients with various indications for IVM. However, the rates of ovarian hyperstimulation syndrome significantly reduced in studies with patients with polycystic ovary syndrome (8). Walls et al. compared fresh, frozen and cumulative cycle outcomes of IVM cycles through an observational study. Their results showed similar success rates, particularly in relation to the incidence of miscarriage in fresh IVM cycles and improved success from frozen embryo transfer (FET) cycles (9).

Conclusion

This is the first case of IVM-TESA ever reported in Turkey and the successful outcome indicates that IVM could be a good alternative in cases of failed conventional ICSI and azoospermia in addition to PCOS and OHSS.

Acknowledgement

We thank Caroline Walker for the English editing.

Conflicts of Interest

All of the authors of this manuscript declare that they have no conflicts of interest.

References

1. Cha KY, Chian RC. Maturation in vitro of immature human oocytes for clinical use. Hum Reprod Update. 1998;4(2):103-20.
2. Chian RC, Tan SL. Maturational and developmental competence of cumulus-free immature human oocytes derived from stimulated and intracytoplasmic sperm injection cycles. Reprod Biomed Online. 2002;5(2):125-32.
3. Mikkelsen AL, Host E, Blaabjerg J, Lindenberg S. Maternal serum supplementation in culture medium benefits maturation of immature human oocytes. Reprod Biomed Online. 2001;3(2):112-6.
4. Fadini R, Colpi E, Mignini Renzini M, Coticchio G, Comi R, Mastrolilli M, et al. Outcome of cycles of oocyte in vitro maturation requiring testicular sperm extraction for nonobstructive azoospermia. Fertil Steril. 2011;96(2):321-3.
5. Son WY, Chung JT, Henderson S, Reinblatt S, Buckett W, Chan PT, et al. Fertilization and embryo development with spermatozoa obtained from testicular sperm extraction into oocytes generated from human chorionic gonadotropin-primed in vitro maturation cycles. Fertil Steril. 2013;100(4):989-93.
6. Trounson A, Wood C, Kausche A. In vitro maturation and the fertilization and developmental competence of oocytes recovered from untreated polycystic ovarian patients. Fertil Steril. 1994;62(2):353-62.
7. Abdul-Jalil AK, Child TJ, Phillips S, Dean N, Carrier S, Tan SL. Ongoing twin pregnancy after ICSI of PESA-retrieved spermatozoa into in-vitro matured oocytes: case report. Hum Reprod. 2001;16(7):1424-6.
8. Sauerbrun-Cutler MT, Vega M, Keltz M, McGovern PG. In vitro maturation and its role in clinical assisted reproductive technology. Obstet Gynecol Surv. 2015;70(1):45-57.
9. Walls ML, Hunter T, Ryan JP, Keelan JA, Nathan E, Hart RJ. In vitro maturation as an alternative to standard in vitro fertilization for patients diagnosed with polycystic ovaries: a comparative analysis of fresh, frozen and cumulative cycle outcomes. Hum Reprod. 2015;30(1):88-96.