Case Report

Live birth from TESA-ICSI in a modified natural cycle – A case report

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Abstract Low ovarian reserve affects 10% of all women seeking fertility treatment. Management of patients with diminished reserve is challenging to fertility experts as they respond poorly to ovarian stimulation, and often such patients resort to oocyte donation. The number of births from natural cycle oocytes with surgically extracted sperm is low, but the case presented here describes a successful case in which a live pregnancy was achieved. In the treatment of a 36-year-old female with bilateral antral follicular count of one to two, two M II oocytes were obtained after modified natural cycle. The husband's semen analysis showed severe infection with occasional dead sperms. The patient did not respond to antibiotics and due to unavailability of sperm on the day of oocyte extraction, the oocytes were vitrified. Sperms were subsequently extracted by TESA. The vitrified oocytes were warmed, and ICSI was performed on the same day. One eight-cell grade I embryo was formed on D3 which was transferred in a programmed hormone replacement cycle. Pregnancy was obtained and a healthy infant was delivered. Hence, in women with low ovarian reserve, the use of modified natural cycle may provide a good alternative to achieving pregnancy prior to considering oocyte donation.

Keywords: IVF, low ovarian reserve, natural cycle, TESA-ICSI

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INTRODUCTION

Low ovarian reserve is the reduced ability of the ovaries to produce oocytes and affects approximately 10% of women seeking fertility treatment.[1] This condition is used to characterize women at risk for poor performance with assisted reproductive technologies.[2-4]

The quantity and quality of ovarian follicles decrease with age.[5] Different trials show that a women has maximum fertility potential in the early 20s.[5] The progressive decline of fertility increases in the late 30s, ending on average age of 50 to 51.[6] The reduction of ovarian function with ageing has been widely defined in term of progressive reduction of ovarian follicles and diminished capability to generate competent oocytes.[7,8] A premature reduction of ovarian reserve can also occur in young age. This condition can be a consequence of chemotherapy, radiation or surgery.[9] However, in 90% of the cases, it is found to be idiopathic.[9]

Several studies show that antral follicle count (AFC) and ovarian volume are very effective in estimating the response to ovarian stimulation.[10] Ovarian antral follicles are evaluated by transvaginal ultrasound at the beginning of the follicular phase of menstrual cycle, and

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the total number of 2 to 10 mm follicles in both the ovaries represents the AFC.[11] AFC with diameter larger than 2 mm are described as 'recruitable', and they are highly sensitive and responsive to gonadotropins.[12]

Management of women with compromised ovarian reserve is challenging for fertility experts and generally the only option to conceive is represented by assisted reproduction technologies (ART).

Women with reduced ovarian reserve yield less oocytes have less embryos for transfer, and their chances of pregnancy are obviously lower.[13] In accordance with European Society of Human Reproduction and Embryology (ESHRE) consensus,[14] patients with reduced ovarian reserve should be defined as 'expected poor responders' to ovarian stimulation during ART cycles. In women with a greatly reduced ovarian reserve, the strategy that provides the greatest chance of pregnancy is represented by egg donation.[15] Natural cycles too can be tried as it allows a natural oocyte selection and an improved embryo quality.[15]

Testicular sperm aspiration or TESA is the most efficient method for retrieving sperm.[16] It requires special expertise and offers a less traumatic method for sperm retrieval.[16] The first attempt at sperm retrieval is the best chance the patient has and gives the highest chance of success with the least morbidity.[16] Fertilization with surgically obtained testicular sperms by intracytoplasmic sperm injection (ICSI) has been successfully used to achieve pregnancies in men with azoospermia.[17] In obstructive azoospermia, 96% recovery rates have been reported using TESA.[17] In non-obstructive azoospermia, reported recovery rates are approximately 50%,[18] although fertilization rates are significantly lower in these men.[19]

Before the advent of ICSI, donor sperm was used for successful fertilization.[20] TESA followed by ICSI circumvents sperm donation in most cases.[20]

As of date, there have been only a few reported cases of TESA followed by ICSI on vitrified oocytes from a modified natural cycle in a patient with low ovarian reserve. Hence, we present a very rare case in which successful pregnancy was achieved and a healthy live infant was born at term.

CASE REPORT

A 34-year-old, regularly menstruating female, married for 3.5 years, presented with a complain of primary infertility. On transvaginal sonography, the antral follicular count was found to be one to two on both the sides, which was correlated with anti-mullerian hormone (AMH) of 1.38 ng/ml. Hormonal profile on D2 was thyroid stimulating hormone (TSH) 1.73 μIU/ml, prolactin 9.62 ng/ml, follicle stimulation hormone (FSH) 6.8 mIU/ml, luteinizing hormone (LH) 5.23 mIU/ml and oestradiol 41.36 pg/ml.

The semen analysis of the male partner demonstrated 0.2 million non-motile dead sperms with plenty of leucocytes. The hormonal profile of the male partner was within normal range as follows: FSH 4.45 mIU/ml, testosterone 142 ng/dl. Antibiotics were prescribed in the hope of resolving the infection and improving the sperm count by the time of oocyte retrieval.

Meanwhile, the patient was stimulated with modified natural cycle and transvaginal follicular monitoring.

She was started on 100-mg clomiphene citrate on the second day of the cycle and on the sixth day of stimulation the dose was reduced to 50 mg when two to three oocytes were observed bilaterally. It was stopped on day 8. On the ninth day of stimulation, the follicular size was 15, 17 and 19 mm, respectively, and Inj. Cetrorelix 0.25 mg [Gonadotropin-releasing hormone (GnRH) antagonist] was started along with human menopausal gonadotropin (hMG) 150 IU. The patient was triggered with Inj. Deca 0.3 mg (GnRH agonist) when the three leading follicles attained the size of >18 mm. Ovum pick up (OPU) was performed 35 h later. Two M II oocytes were obtained. However, the male partner was not able to produce a semen sample on the day of oocyte retrieval due to high grade fever. Hence, ICSI could not be performed and the M II oocytes were vitrified 2 h after retrieval. The Cryotop method for oocyte vitrification was used. An improvement in semen parameter was expected after treatment with antibiotics, but a repeat semen sample was performed after a month demonstrated azoospermia. So, surgical retrieval of sperm was planned. In azoospermia, there will be no sperm in the epididymis. Hence, testicular sperm retrieval was planned at a later date.

A programmed hormone replacement cycle was started for the patient in the next cycle from day 3 of menses. She was started on oral E2 (tablet progynona, oestradiol valerate) 4 mg and the dose was increased to 6 mg on day 6. On the ninth day of endometrial preparation, the endometrial thickness was found to be 11 mm, and a triple-line pattern was observed on ultrasound. The patient was started on 800 mg of vaginal progesterone suppositories in two divided doses daily for 3 days and TESA was performed. Few viable sperms were obtained and, ICSI was performed after warming the vitrified oocytes. One eight-cell grade I embryo was formed on day 3 and transferred using Labotect cannula, under abdominal ultrasound guidance.

Oral E2, vaginal progesterone, injectable progesterone, low-dose aspirin, multivitamins, folic acid and antacids were prescribed, and the woman was called after 14 days for urine pregnancy test. On the 14th day, the urine pregnancy test was found to be positive which was confirmed with serum beta human chorionic gonadotropin (β-hCG) of 526.0 mIU/ml. The hormonal supplementation was continued until 12 weeks of gestation. She had an uneventful antenatal period and delivered at term by normal vaginal delivery. She gave birth to a healthy 2.8-kg female baby.

DISCUSSION

The first report that investigated the natural cycle as a first strategy in women with low prognosis related to age and diminished ovarian reserve. It was performed by Papaleo *et al*. They found a similar pregnancy rate to that of conventional in vitro fertilization (IVF) in older women.[21] Schimberni *et al*. evaluated 500 natural cycles followed by ICSI in poor responders. They observed that natural cycle IVF to be an efficacious protocol for poor responders, especially younger women.[22]

However, the use of natural cycles presents some disadvantages mainly due to the frequent spontaneous LH surge, the resulting high cancellation rate (up to 30%), the difficulties in programming oocytes retrievals, the high incidence of failure to recover oocytes during oocyte pick-up (16.7%–71.4%) and low pregnancy rate per embryo transfer cycle (0%–23.5%).[23]

Hence, modified natural cycle may be a more prudent approach to patients with low ovarian reserve. Modified natural cycle protocol means GnRH antagonist administration when a follicle attains 14 mm on ultrasound, with the daily addition of FSH or hMG, to support additional follicular growth.[24]

Yoo *et al*. compared IVF outcomes of mild ovarian stimulation with conventional ovarian stimulation in poor responders. They found a higher pregnancy rate in women who were recommended modified natural cycle stimulation protocols.[25] In addition, modified natural cycles IVF is a relatively easy procedure, especially for patients, that minimizes physical and emotional stress, the costs of treatment and laboratory tests.[26] Natural cycle IVF allows a natural oocyte selection and an improved embryo quality.[27] A case report by Akagbosu *et al*.[28] and a paper by Aboulghar *et al*.[29] suggest a negative impact of conventional IVF on oocyte quality. So, in our patient, our first approach was to try a modified natural cycle before considering other approaches, and we found that we were able to recruit three follicles and obtained two good-quality oocytes (M II).

The quality of the oocyte was confirmed by a good embryo formed even with TESA sperm. A study by Kalliopi *et al*. found that fertilization and cleavage rates, quality of embryos as well as blastocyst development rates were significantly reduced with TESA sperms.[30] A possible explanation for this may be that testicular spermatozoa are less mature and subsequently less competent to fertilize than the ejaculated ones, as the final step of sperm maturation takes place in the epididymis.[31] Embryo development can also be influenced by the quality of DNA in the sperm head. Testicular sperms have abnormal chromatin packing in the sperm head and hence lead to abnormal chromatin de-condensation at fertilization.[16,32] It is speculated that oocytes have the ability to correct small-scale DNA damage upon fertilization.[32] The eggs obtained in our minimal stimulation natural cycle gave a good embryo and a live pregnancy even with a TESA sperm.

CONCLUSION

A good number of women with low ovarian reserve may conceive with their own eggs, if they are stimulated by modified natural cycle. Modified natural cycle yields good-quality eggs and embryos as compared to stimulated cycles in patients with low ovarian reserve and hence should be tried prior to considering egg donation. It is cost effective and has less psychological and financial burden for the patient.

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Conflicts of interest
There are no conflicts of interest.

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