

## Original Article

# Twin pregnancy after intracytoplasmic sperm injection in woman aged 49 using autologous oocytes by mild ovarian stimulation: a case report

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**Abstract:** There were few reports about infertile women aged 45 and above undergoing IVF/ICSI. We are reporting the case of an aged 49 woman who delivered the twins after ICSI using autologous oocytes by mild ovarian stimulation. The patient presented with 26-year primary infertility caused by double fallopian tubes obstruction and man oligoasthenozoospermia. We gave her the treatment with mild ovarian stimulation cycle of clomiphene citrate (CC) and follicle stimulating hormone (FSH) undergoing ICSI, and transferred two fertilization-blastocysts. The outcome measured was the live birth. The twins were delivered by cesarean section operation at 37 pregnancy weeks for the moderate pregnancy-induced hypertension. In summary, we found it is feasible for women with advanced age to undergo ART while the accompanied risk of pregnancy complications and other issues need to be further evaluated.

**Keywords:** Advanced age, autologous oocytes, mild ovarian stimulation, endometrial receptivity

## Introduction

The number of women over 40 years of age seeking infertility treatment has been steadily increasing in the past decades [1]. The percentage of women over 40 requiring assisted reproductive technology (ART) has increased significantly up to 25% in 2009 [2]. There has been great interest in the reproductive capacity of women in their late reproductive years. But published studies report a clinical pregnancy rate of 10~15% in women over 40 undergoing IVF or ICSI [3]. In our center, from January 2012 to December 2014, a total of 79 IVF/ICSI cycles in women over 40 years were attempted to 425 oocytes retrievals, with the ovarian stimulation failure of 15%. Up to date, the declining fertility of women aged  $\geq 40$  years who are using their autologous oocytes is an individual event. The bulk of research pertaining to infertility has focused on women below aged 45, but there was few report about infertile women aged 45 and above [1]. We present the case of an aged 49 woman presenting with primary infertility.

## Methods

A 49-year-old woman presented with a 26-year history of primary infertility in March 2013. The

patient's husband had an oligoasthenozoospermia analysis (WHO). The patient was screened by transvaginal ultrasound and serum FSH testing on day 3 of their menstrual cycle. Basal follicle-stimulating hormone (FSH) levels was 32 IU/L, antral follicle count (AFC) were only two. Considering the poor response, we gave her the mild ovarian stimulation protocol as Clomiphene citrate (Fertilan; Codal-Synto Ltd., France) 100 mg/day co-treatment with and 150 IUHP-FSH (Li shenbao, Livzon Group Pharmaceutical Factory, China) from cycle day 3 onwards. But there was no dominant follicle development. The next cycle nature cycle had no dominant follicle development. Until the third cycle, the patient underwent the same protocol as the first cycle, the number of follicles  $>14$  mm were 3 on the HCG day. Transvaginal ultrasound guided OPU was performed 36 hours after 8000U hCG administration. We performed ICSI with each ejaculated sperm. There were 2 blastocysts (3BB, 3BB) on day 5. Because of the endometrial factors, we cancelled the fresh transfers. Soon afterwards, the patient received the hysteroscopic resection endometrial polyps and the herbal treatment. Until July, 2014, under the nature cycle with in perfect endometrium condition,

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two fertilization-blastocysts were transferred. The patient received daily luteal phase support, in the form of 20 mg/IM, Qd, of progesterone (Tongyong, Co, Shanghai, China), Dydrogesterone Tablets 10 mg/PO, Bid (Abbott Healthcare Products B.V, Netherlands) from the day of 5 days before ET day. Follow-up was accomplished by telephone communication for additional information up to today (2 month after delivery). The study protocol was approved by the Ethics Committee (Institutional Review Board) of the Tongji Hospital of Shanghai, Chinese IVF-ET Center, and there were no conflicts of interest for any of the authors.

### Results

11 days after ET day, the blood human chorionic gonadotropin ( $\beta$ -hCG) rose up to 1427 mIU/ml. and 16 days later, transvaginal ultrasound reported the "intrauterine twins". On March 7th, 2015, at the 37 pregnancy weeks, the twins were delivered by C-S operation for the patients suffered from the moderate pregnancy-induced hypertension. The weight of the twin girls were 2250 and 2350 respectively. The follow-up was up to today showing that both mother and the twins were normal.

### Discussion

Age of the woman is the most important factor in determining pregnancy success rates, whether in natural conception or after ART, which mainly attributed to a decrease in egg quality. Despite the low pregnancy and live-birth rates in women aged  $\geq 40$  years who were using autologous oocytes, the percentage of these infertile women asking for this line of treatment in IVF programs is increasing, particularly in countries where egg donation is a cultural, religious, or ethical issue that limits or prohibits its application. Furthermore the physical, emotional, and financial burdens of ART on the couple cannot be ignored.

The largest study [4], a single center experience in 2386 initiated cycles of IVF-ICSI in 1645 women aged  $\geq 40$  years showed that the cancellation rate was 16% per initiated cycle, and there was a linear increase in the cancellation rate at 1-year age increments, with a sharp rise of cancellation rate at age 45 and above whose overall clinical pregnancy rate being 13.4% with the live-birth rate 6.7% per initiated cycle. At 44 years of age, the pregnancy loss rate may reach to 75%.

The outcome of the IVF-ICSI cycles in our study showed that it was not clinically appropriate to initiate an IVF-ICSI cycle once the patient is 43 years old.

So, Women aged  $\geq 43$  years should be discouraged from undergoing IVF in favor of egg donation if it is ethically and culturally acceptable. While, good response in their first attempt should be encouraged to have repeat cycles.

How to choose the stimulus protocols suitable to patients older than 40 with a diminished ovarian reserve? Compared to classical protocols, mild stimulation with low dose of gonadotropins under antagonist is an interesting alternative for patients with poor ovarian reserve, which may produce more good quality embryos, better implantation and pregnancy rates when the same number of embryos was transferred [4]. That is to say, mild stimulation could be a beneficial option to patients over 40 years. In our study, we chose the mild stimulation to gain 3 matured eggs with the total Gn1050IU.

Improving the implantation rate was another key factor in the ART procedure. While, embryo implantation involves many factors, among which was endometrial receptivity which accounting for two third failures. But how to improve the endometrial receptivity was a following key question. Reports showed that endometrial scraping during menstrual period could improve the embryo implantation and endometrial receptivity [5], so as the patient in our study, we implement the menstrual scraping to improve her endometrium.

Advanced age is the independent risk factor of many pregnancy complications. Simultaneously, multiple pregnancy was another pregnancy risk factor. So, multifetation reduction to twins or singleton is associated with improved outcomes. But in our study, the patient refused the reduction and required to retain twins. We advised her to receive the close obstetric follow-ups to ensure the peace maternal and child.

### Disclosure of conflict of interest

None.

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