

# Multiple artificial insemination failure in a case of unexplained infertility

Dorina Codreanu, MD, Andreea Vultur, MD, Laura Dracea, MD, Manuela Neagu, MD, PhD, B. Marinescu, MD, PhD

Clinical Hospital of Obstetrics-Gynecology  
"Prof. Dr. Panait Sărbu", Bucharest  
Assisted Human Reproduction Department

Correspondence:  
Dorina Codreanu  
e-mail: dorina\_73@yahoo.com

## Abstract

*In planning the treatment policy of unexplained infertility over-treatment should be avoided, thereby minimizing the health risks and the total cost of the treatment. Therefore, intrauterine insemination either in natural or stimulated cycle is used as a first line treatment.*

*This paper presents the case of a couple with primary unexplained infertility and repeated intrauterine insemination (IUI) failure. A rare cause of infertility was revealed by their first IVF attempt.*

**Keywords:** *intrauterine insemination, unexplained infertility, IVF*

## Introduction

Artificial insemination is the first line treatment in case of unexplained infertility, being much less invasive and cheaper than in vitro fertilization. Conception rate is about 10-17% per cycle with 85% of the pregnancies achieved in the first 4 insemination cycles<sup>1</sup>. Six insemination cycles are generally recommended before moving to in vitro fertilization, excepting women over 37 years of age, the possibility existing,

in their case, for in vitro fertilization to be proposed sooner or even as the first option.

## Case report

A patient called C.M., age 31 and her husband C.L., age 37, presented in our clinic in March 2000 to investigate a primary couple infertility of about 3 years. The couple started until presentation in our clinic a series of summary investigations in another center (general and genital clinical

examination, semen analysis and basal body temperature monitoring), as well as a series of ovarian stimulations with clomiphene citrate in 3 consecutive cycles.

Investigations done in our clinic couldn't highlight an infertility cause:

- **female partner:** regular menses, normal ovulatory status confirmed by transvaginal ultrasound and hormonal determinations (FSH, LH and estradiol in

the early proliferative phase and progesterone in the mid-luteal phase), normal thyroid function, normal serum prolactin, negative chlamydia, mycoplasma and ureaplasma tests, without a history of a pelvic inflammatory disease;

- **male partner:** semen analysis done in clinic ( $84 \times 10^6$  spz/ml, 72% progressive mobility A+B and  $\geq 60\%$  normal morphology spermatozoa) was within normal parameters according to WHO criteria.

Given these data and the relatively young age of the patient, to improve the fertile prognosis, we recommended artificial insemination with spouse's semen (IUI) in natural cycle (not stimulated). In 2001, the patient had 4 IUI in natural cycle with ultrasound monitoring of ovulation (all cycles were ovulatory) and inseminations done 35-38 hours after ovulation triggering with 5000 UI Pregnyl.

The couple didn't achieve pregnancy and therefore more thorough investigations were decided: hysterosalpingography (HSG) was done, which showed normal uterine cavity and bilateral tubal permeability; and semen analysis, hormonal determinations and chlamydia tests were repeated (all within normal limits). It was decided then an active approach using data from the literature that postulates a higher rate of pregnancy after insemination in stimulated cycle versus the natural cycle in unexplained infertility. The patient undergone 3 IAS in stimulated cycle with 50 mg clomiphene citrate and other 3 in which estroprogestogens were added (2 mg estrofem, orally, from the 8th day of the cycle and until hCG was given and 400 mg micro-

nized progesterone, vaginally, from the second day after insemination) to suppress the negative effects of clomiphene on the endometrium. In all 6 cycles of insemination performed between March 2003 and May 2004 the patient had 1-3 follicles between 16 and 21.5 mm in diameter and trilaminar endometrium pattern of 9-12 mm thick at hCG trigger time. All 6 inseminations were ineffective.

After 4 years and 9 failed IUI, in October 2004 exploratory laparoscopy was done showing normal pelvis without adhesions and without implants of endometriosis, 2 ovarian follicular cysts bilaterally under 2-3 cm in diameter which were discharged by drilling with monopolar electrocautery, uterus and both tubes with normal appearance and bilateral tubal permeability on upward testing with methylene blue. Immediately after, both partners carried out genetic tests that showed normal karyotype without numerical or structural chromosomal abnormalities.

Given the multiple IUI failure and the patient age, now over 35 years, use of in vitro fertilization was recommended, a procedure that the patient couldn't follow on because of financial reasons. Between March 2005 and June 2008 the couple performed 5 IUI, both in natural and stimulated cycle.

In August 2008, after 14 unsuccessful IUI cycles in 8 years, the patient now aged 39 starts investigations to enter IVF program. The procedure was performed in October 2008 and consisted in ovarian stimulation with 225 UI FSH after prior pituitary desensitization with 0.1 mg decapeptyl administered from day 21 of the previous cycle (long protocol). Contrary to expectations with re-

gard to patient age, ovarian response to stimulation was a very good one and, after 11 days of stimulation and induction of final oocyte maturation with 10000 UI pregnyl, 16 mature oocytes were extracted by ultrasound guided vaginal puncture. Subsequent developments brought the answer on why pregnancy wasn't achieved so far: 24 hours after incubation of oocytes with spouse's semen, total fertilization failure was found. The ICSI procedure done after finding this didn't lead on getting a single viable embryo.

### Discussions :

Total fertilization failure is a rare and unexpected event in cases in which semen analysis is normal. On couples with infertility of an unexplained cause, incidence is greater than on couples who resort to IVF because of tubal factor infertility.

The causes of fertilization failure are found in most cases at the spermatozoa level (hidden defects that cannot be revealed by conventional semen analysis, but require functional tests of fertilizing capacity)<sup>2</sup> but can also be found at the oocyte level, in very rare cases<sup>3</sup>.

### Conclusions

Repeated failure of assisted human reproduction procedures is frustrating for both couples and medical team.

Not only male subfertility but also unexplained infertility are risk factors for total fertilization failure at the first IVF attempt.

We believe that in cases with previous repeated unexplained IUI failure, intracytoplasmic sperm injection (ICSI) is useful for at least some of the oocytes at the first IVF attempt. ■

### References

1. Nuojua-Huttunen S, Tomas C, Bloigu R, Tuomivaara L, Martikainen H. Intrauterine insemination treatment in subfertility: an analysis of factors affecting outcome. *Hum Reprod* 1999; 14:698-703.
2. Lee TH, Liu CH, Huang CC, Chen HH, Chen SU, Lee MS. The association between polypronucleate zygote formation with certain motion characteristics of sperm and IVF outcome. *J Assist Reprod Genet.* 2008 Jan;25(1):35-41. Epub 2008 Jan 19.
3. Gasca S, Reyftmann L, Pellestor F, Rème T, Assou S, Anahory T, Dechaud H, Klein B, De Vos J, Hamamah S. Total fertilization failure and molecular abnormalities in metaphase II oocytes. *Reprod Biomed Online.* 2008 Dec;17(6):772-81.