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CASE REPORT

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A report of two cases with successful oocyte retrieval after wrongly earlier injection of ovulation induction trigger: Case report

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Abstract

Oocyte maturation is induced by trigger administration and is acritical step in the success of assisted reproductive technology (ART)treatment. The ideal time interval between trigger administration and oocyte retrieval varies in the literature. Extremely short or long time intervals are both knownto cause unfavorable outcomes in oocyte collection. Accurate control over theinterval between trigger injection and oocyte retrieval is very important forwomen undergoing in vitro fertilization (IVF), to avoid unexpected premature ovulation.

In this report, we present two infertile women who mistakenly injected the triggering dose of gonadotropin releasing hormone agonist (GnRHa) 12 h earlier. Case 1 and case 2 were 23 and 30 years old, respectively. Therewas no intervention to prevent pre-operative ovulation, and oocyte retrievalhas been done 48–50 h after trigger injection. oocytes and embryos quality wereacceptable.

In conclusion, in patients who have the wrong trigger injection, oocyte retrieval is recommended after consulting the patient about theadvantages and disadvantages of the oocyte retrieval operation.

KEYWORDS

assisted reproductive technology, GnRHa triggering, oocyte maturation, oocyte retrieval

1 | BACKGROUND

Induction of oocyte maturation in controlled ovarian stimulation (COS) cycles is done using human chorionic gonadotropin (hCG) or GnRHa to prevent the development of ovarian hyperstimulation syndrome (OHSS). In the maturation process, the oocyte gains competence for fertilization that is a critical step in the success of ART. Oocyte maturation is initiated by luteinizing hormone (LH)-like exposure that can be provided by hCG, GnRHa, recombinant LH, or kisspeptin.[1] In the natural cycle, endogenous LH surge usually lasts for 48 h and ovulation occurs between 37 and 39 h after the onset of LH surge.

The ideal time interval between hCG administration and oocyte retrieval varies in the literature. Extremely short- or long-time intervals are both known to cause unfavorable outcomes in oocyte collection. There is a case report in the literature that the patient injected the trigger 9 h earlier than scheduled triggering. They have done an intervention to prevent preoperative ovulation

after incorrect trigger injection to the night before oocyte pick up. The result showed that preoperative ovulation was effectively prevented and they successfully collected the expected number of oocytes.[2] In the present cases, there was no intervention to prevent preoperative ovulation, and oocyte retrieval has been done 48–50 h after the triggering.

In this report, we present two cases who mistakenly injected the triggering dose of GnRHa 12 h earlier. In ART treatment cycles, oocyte retrieval is generally performed around 36 h after the administration of ovulation-triggering drugs. When the time interval between the administration of ovulation trigger and oocyte retrieval becomes longer, there is a concern about follicle rupture and oocyte aging.

2 | CASE PRESENTATION

2.1 | Case 1

A 23 years old woman was trying to conceive for nearly 2 years without success. Her menstrual periods were irregular and the periods occured at an interval of 2 months. Her body mass index (BMI) was 29 kg/m^2 and there was no dysmenorrhea. Cervical smears were normal and there was no history of sexually transmitted infection. Evaluation of fallopian tubes with hysterosalpingography (HSG) showed normal results. There was no pathological finding in the general and gynecological examination. Her 25-year-old partners' semen analysis showed azoospermia. On day 20 of the previous cycle, 4 mg of estradiol was started for the patient. Ovarian stimulation was started by injection of 150 IU recombinant follicle-stimulating hormone (FSH) (Cinal-f, Cinnagen, Iran) on day 2 or 3 of the menstrual cycle. The first sonography was done on day 6 after the beginning of recombinant FSH. GnRH antagonist (cetrotid 0.25 mg, Merck, Germany) was added when there was a follicle greater than 14 mm. In addition, daily 75 to 150 IU of human menopausal gonadotropin (hMG) (PD homog, pooyesh daru, Iran) was started. Sonography was performed every 3 days. When there were two follicles greater than 18 mm, GnRHa (decapeptyle 0.2 mg, Ferring, Switzerland) was administrated as a trigger to prevent OHSS. We planned to retrieve oocytes 36 h after injection of the trigger. Unfortunately, the patient injected the trigger at 8 AM instead of 8 PM. Oocyte retrieval was done 48 h after injection of GnRHa. We retrieved 29 oocytes and freeze them because no sperm was obtained from the testicular biopsy of the partner. Twenty-two oocytes were in the metaphase II (MII) stage, 6 oocytes were in the metaphase I (MI) stage, and one oocyte was in the germinal vesicle (GV) stage. MII oocytes did not display the appearance of postmaturity, like extremely expanded cumulus masses, darkened corona radiate, atretic cumulus cells, and fragmented polar bodies. Estradiol and progesterone on the day of trigger administration were 3450 pg/mL and 2.62 ng/mL, respectively.

2.2 | Case 2

A 30 years old woman with 5 years of primary infertility was seen in the gynecology clinic of X. The partner had no previous medical history of note. The woman also has no specific previous medical history. Her periods were every 35–60 days and were sometimes heavy but not painful. There was no inter-menstrual or postcoital bleeding. She had normal cervical smears and never had any sexually transmitted infections. On examination day, her BMI was 28 kg/m^2. Speculum and bimanual examination were normal. She had an IVF failure 1 year ago. Her partner's semen analysis showed mild asthenozoospermia and he had no past medical history. Also in this patient, the treatment protocol used for COS was similar to Case 1. Similar to the first case, GnRHa was used as a trigger but it was injected at 9 AM instead of 9 PM mistakenly. Oocyte retrieval was done 48 h after injection of GnRH agonist and 15 oocytes were retrieved. Eleven oocytes were in the MII stage, 1 in the GV stage, and 3 degenerated oocytes. After intracytoplasmic sperm injection (ICSI) 9 grade A embryos were obtained. Estradiol and progesterone on the day of trigger administration were 3260 pg/mL and 2.4 ng/mL, respectively. Transfer of embryos had not been done because of the OHSS.

3 | DISCUSSION

Administration of hCG at midcycle has been the gold standard for triggering final oocyte maturation and ovulation in ART cycles. More recently, GnRHa triggering has been introduced to allow a more physiologic surge of both LH and FSH. This combined surge may result in improved oocyte and embryo quality and prevent the development of OHSS.[3] Accurate control over the interval between trigger injection and oocyte retrieval is very important for women undergoing IVF, to avoid unexpected premature ovulation. Serum progesterone level >3 ng/mL and free fluid in the pelvis (or pouch of Douglas) are signs of ovulation occurrence.[4] In the present cases, serum progesterone levels were <3 ng/mL, and no free fluid was seen in the pelvis. Therefore, it seems ovulation did not occur in these cases. In addition, retrieved oocytes did not display the appearance of post-maturity, like extremely expanded cumulus masses, darkened corona radiate, atretic cumulus cells, and fragmented polar bodies.

In a case report presented by Cheng and Li[2] that patient was injected with trigger 9 h earlier than the scheduled triggering. To prevent preoperative ovulation, indomethacin was given (150 mg/day, three times a day) from 2 h after incorrect trigger injection to the night before oocyte pick up. The result showed that preoperative ovulation was effectively prevented and they successfully collected the expected number of oocytes at 45 h after triggering. However, in our cases, there was no intervention to prevent preoperative ovulation, and oocyte retrieval has been done 48–50 h after trigger injection. We found out the mistake made by the patient on the day of oocyte pick up. So, we could not schedule an earlier oocyte pick up, however, we prioritized these two patients for oocyte pick up and retrieved their oocytes as soon as possible. Interestingly, oocytes and embryos quality were acceptable. These results show that in patients who have the wrong trigger injection, oocyte retrieval is recommended after consulting the patient about the advantages and disadvantages of the oocyte retrieval operation. This is an important issue in IVF clinics because COS has a high cost and side effects for the patients. However, there is a need for further studies to assess the effect of the different time intervals between triggering and oocyte retrieval on oocyte number and quality.

AUTHOR CONTRIBUTIONS

Roya Kabodmehri: Conceptualization; data curation; supervision; writing – review and editing. **Seyedeh Hajar Sharami:** Supervision; writing – review and editing. **Nasrin Ghanami Gashti:** Methodology; writing – original draft; writing – review and editing. **Mohammad Hadi Bahadori:** Data curation; writing – review and editing. **Ziba Zahiri Sorouri:** Conceptualization; data curation; methodology; writing – review and editing.

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None.

CONFLICT OF INTEREST STATEMENT

The authors declare that they have no conflict of interest.

DATA AVAILABILITY STATEMENT

Supporting data are available in Reproductive Health Research Center Department of Obestetrics and Gynecology Al-zahra Hospital/School of Medicine/Guilan university of Medical Sciences/Rasht/Iran.

ETHICAL APPROVAL

Ethical approval was obtained from the ethics committee of Guilan University of Medical Sciences (Approval ID: IR.GUMS.REC.1400.333).

CONSENT

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

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