Case Report

Recurrent empty follicle syndrome with different stimulation protocols – A case report

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Abstract

We report a case of recurrent empty follicle syndrome (EFS) where no oocytes were aspirated in two separate IVF cycles using two different protocols. In the second cycle, oocyte aspiration in one ovary was delayed for 24 hours after administering a second dose of human chorionic gonadotropin injection (hCG) and still no oocytes were recovered. In view of the presence of severe male factor infertility and failure to retrieve oocytes in 2 stimulated cycles, the couple was offered donor embryo transfer which resulted in a singleton pregnancy. A baby girl weighing 2800 g was delivered by an elective caesarean section at term. This case highlights that the change of protocol or repeat hCG administration is unlikely to change the outcome of genuine empty follicle syndrome.

Keywords: Empty follicle syndrome, in-vitro fertilization, ovarian stimulation, recurrent empty follicle syndrome, stimulation protocols

Introduction

Empty follicle syndrome (EFS) is defined as failure to retrieve oocytes from mature ovarian follicles following ovulation induction for In-vitro Fertilization (IVF) and meticulous aspiration with repeated flushing despite normal ovarian follicular development and adequate oestradiol levels. This phenomenon was first described by Coulam *et al.* in 1986.[1] The incidence of EFS has been variably reported between 2-7%.[1]

The aetiology of empty follicle syndrome is unknown. Ovarian aging, abnormal folliculogenesis with early oocyte atresia and delayed maturation of oocyte-cumulus complex (OCC) in response to hCG trigger are suggested possible mechanisms.[1,2] Inherited mutation of LH/chorionic-gonadotrophin receptor (LHCGR) has been reported in patients with EFS.[3]

Case Report

A 34-year-old woman presented to gynecology clinic with a history of primary subfertility for 10 years. She had undergone emergency laparotomy and ovarian cystectomy in 2008. The histology confirmed a corpus luteal cyst. In 2010, a laparoscopy and dye test confirmed normal pelvic anatomy and tubal patency.

Husband's seminal fluid analysis confirmed severe oligoasthenoteratozoospermia. In view of the abnormal seminal fluid parameters, the couple was advised to undergo in-vitro fertilization and embryo transfer. Her basal FSH level was 5.71 miu/ml indicating a good ovarian reserve.

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She underwent the first IVF cycle with the antagonist protocol. Ovarian stimulation was achieved with gonadotropins (Follitrophin beta -Recagon) and patient developed 35 follicles. Serum oestradiol level on day 8 of stimulation was 1004 pg/ml. Once the mature follicles were seen 10, 000 IU of hCG was administrated and oocyte pick-up (OPU) was performed 35 hours later. No oocytes were retrieved.

The second cycle was commenced 3 months later with long pituitary down-regulation protocol using GnRH agonist (Decapeptyl). Ovarian stimulation was achieved with gonadotropins (Follitropin alfa - Gonal F). The patient developed 40 follicles in both ovaries. Serum oestradiol level on day 8 of stimulation was 944 pg/ml. Once the follicles were mature 10,000 IU of hCG was administrated and oocyte pick-up (OPU) was performed after 35 hours. On the day of OPU, 30 follicles were aspirated and no oocytes were retrieved. Rest of the 10 follicles were aspirated 24 hours later after repeat 10,000 IU hCG administration under direct supervision. The serum beta hCG prior to egg retrieval was 185 mIU/ml indicating satisfactory hCG concentration. Still no oocytes were retrieved.

In view of repeated failure to retrieve oocytes in both IVF cycles and severe male factor infertility, she was offered donor embryo replacement 9 months after the second cycle. Following donor embryo transfer, she was pregnant and the pregnancy progressed normally. She delivered a baby girl weighing 2800 g by an elective caesarean section.

Discussion

Empty follicle syndrome is a rare condition which could recur in spite of using different ovarian stimulation protocols. Two types of EFS are described in literature. Genuine Empty Follicle Syndrome (GEFS) is the inability to retrieve mature oocytes following apparently normal folliculogenesis and steroidogenesis in the presence of optimal serum concentration of beta hCG on the day of oocyte retrieval.[4] False Empty Follicle Syndrome (FEFS) is when oocytes not retrieved with suboptimal serum concentration of beta hCG.[4] FEFS is unlikely to recur in the subsequent stimulation cycles.[4]

Our patient had 2 cycles of ovarian stimulation for IVF, using both agonist and antagonist protocols. In the second cycle, there were 2 attempts of oocyte retrieval; the second attempt after a rescue administration of 10,000 IU hCG with adequate hCG concentration prior to oocyte pick up. In both instances, there was no oocyte yield. Therefore, this patient can be recognized as a case of GEFS.

Reported management of FEFS include repeat administration of hCG, administration of recombinant hCG, recombinant LH and triggering oocyte maturation with GnRH agonist in antagonist cycle with variable results.[2,4,5] Estimated risk of recurrence of EFS is 20%. Risk of recurrence is higher with increasing age of the female partner.[1,6] Therefore, patients with an EFS cycle should be counseled regarding the risk of recurrence of this syndrome and reduced pregnancy rate in subsequent IVF cycles.

The etiology and the optimal management of this syndrome still remains an enigma. Assisted reproduction using donor eggs and donor embryo transfer are acceptable alternative management options for recurrent EFS. Our patient was offered donor embryo transfer since there was severe oligoasthenoteratozoospermia in the male partner. Awareness about these rare causes of subfertility is important for all categories of medical staff since patients could present to them for advice.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interests

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