CASE REPORT

The development of an oocyte-containing follicle during gonadotrophin-releasing hormone agonist administration

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Administration of gonadotrophin-releasing hormone (GnRH) agonist in a 29 year old woman with infertility due to ovulatory dysfunction resulted in the development of several ovarian cysts. After human chorionic gonadotrophin (HCG) was injected, the cysts were aspirated and one mature oocyte was retrieved. Intracytoplasmic sperm injection (ICSI) was performed and the resulting embryo was transferred. A singleton pregnancy was obtained and a healthy baby was born at 36 weeks of gestation. Because GnRH agonist-derived cysts may contain oocytes, we suggest that when the growth of cysts is accompanied by high concentrations of oestradiol, the administration of HCG may be useful to achieve oocyte maturation and advance IVF treatment.

Key words: follicle development/GnRH agonist/ICSI

Introduction

The use of gonadotrophin releasing hormone (GnRH) agonist in IVF cycles is associated with an estimated 5% incidence of ovarian cysts (Jenkins, 1996; Mehta and Anand Kumar, 2000). The risk of cyst formation increases in women with ovulatory dysfunction (Feldberg et al., 1989; Lockwood et al., 1995; Jenkins, 1996; Ellenbogen et al., 1997; Mehta and Anand Kumar, 2000), and when GnRH agonist treatment is initiated at the follicular rather than the luteal phase of the menstrual cycle (Lockwood et al., 1995; Mehta and Anand Kumar, 2000).

The formation of ovarian cysts following pituitary down-regulation is considered detrimental. Thus, in many cases IVF cycles are cancelled or cysts are aspirated to discontinue their functional activity (Feldberg et al., 1988; Rizk et al., 1990; Silverberg et al., 1990; Jenkins et al., 1992; Ellenbogen et al., 1997).

In this case report we present a woman with impaired ovarian function, who developed an oocyte-containing cyst upon GnRH agonist administration. Following the use of HCG and ICSI, a successful pregnancy was established.

Case Report

A 29-year-old woman presented with 5 years of primary infertility and 2 years of secondary infertility due to ovulatory dysfunction (menstrual bleeding every 30–90 days) and husband's oligoasthenospermia. The patient's LH and FSH concentrations were 15 IU/l and 10.4 IU/l respectively (upper limits of normal levels). Prolactin, thyroxine and thyroid stimulating hormone (TSH) were normal. Polycystic ovaries were indicated by sonography.

Three years previously, an IVF treatment (14 oocytes retrieved, 50% fertilization) combined with zygote intra-Fallopian transfer had resulted in a pregnancy and the birth of a healthy boy weighing 2970 g. During the last 2 years, two IVF cycles were attempted (23 and 18 oocytes were achieved with 48% and 39% fertilization rates respectively), but the woman did not conceive. On day 21 of the menstrual cycle preceding her treatment cycle, oestradiol and progesterone concentrations were 200 pmol/l and 1.9 nmol/l respectively. Transvaginal sonography revealed small follicles and GnRH agonist (Decapeptyl CR 3.75 mg; Ferring, Kiel, Germany) was initiated. Eleven days later, oestradiol and progesterone concentrations were 5276 pmol/l and 3.0 nmol/l respectively. Sonography revealed seven follicle-cysts (2.0–2.4 cm in diameter) and the endometrial thickness was 6 mm. The woman expressed her wish to have the cysts aspirated in order to advance her treatment. She agreed to our suggestion to attempt HCG administration in case the follicles contained oocytes. HCG (10000 IU; Chorigon, Teva, Kfar Savah, Israel) was administered and 36 h later the follicle-cysts were aspirated. The aspirates were examined and a single oocyte was retrieved. Because the husband had a low concentration of motile sperm (a total of 0.8×10⁶ spermatozoa with poor motility) and because we were concerned that IVF insemination of a single oocyte might result in failed fertilization, ICSI was performed. We suggested to our patient the option of freezing the single embryo for a later transfer along with other fresh...
or frozen embryos but the women preferred to complete the treatment. After ~48 h a 4-cell embryo was transferred into the uterus. On the day of embryo transfer endometrial thickness was 9 mm and serum oestradiol and progesterone concentrations were 1402 pmol/l and >130 nmol/l respectively. Daily injections of 100 mg i.m. progesterone (Geston; Pains and Byrne, Surrey, UK) were provided for luteal phase support. The woman conceived and a healthy baby boy weighing 2800 g was born at 36 weeks of gestation.

Discussion
The use of GnRH agonist has been associated with an increased incidence of functional ovarian cysts. The mechanisms of cyst formation during pituitary down regulation are not yet clear. It has been suggested (Ron El et al., 1989) that the transient stimulatory phase induced by GnRH agonist may stimulate follicles to grow but due to the rapid pituitary desensitization their development is arrested and ovulation does not occur. An additional hypothesis was presented on the possible correlation between GnRH agonists and cyst formation (Mehta and Anand Kumar, 2000). They reported a case that supports the hypothesis that GnRH agonists directly affect ovarian steroidogenesis. However, our case indicates that follicular development may occur during GnRH agonist treatment, thus supporting the hypothesis that GnRH agonists induce transient pituitary flare-up (Ron El et al., 1989). We surmise that some follicles (one out of seven in the present case) may become highly sensitive to short-term stimulation by gonadotrophins and this may result in oocyte development. Whether, as in our case, the oocyte-containing cysts develop primarily in polycystic ovaries remains yet unanswered. It is noteworthy that GnRH agonist induced ovulation has been shown in a woman with hypergonadotrophic amenorrhoea (Check et al., 1988). Because our patient had high normal concentrations of FSH and LH, it seems that the formation of follicles containing oocytes in response to GnRH agonist may also be anticipated in women with elevated endogenous gonadotrophins.

It seems that the GnRH agonist did not impair oocyte quality and endometrial receptivity because normal fertilization was enabled and embryo implantation was successful. The inhibitory effect of GnRH agonist on corpus luteum activity was overcome by progesterone administration.

The procedure presented in this report may be considered as a treatment option when follicle-cysts to be aspirated are accompanied by a significant rise in circulating oestradiol concentrations. However, the practice is suboptimal because the oocyte yield might be low, thus affecting the final outcome of the treatment. Being aware of the large resources required to complete an IVF cycle, we suggest that this procedure should be applied in carefully selected cases and combined with the option of embryo cryopreservation.

References

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