SHORT COMMUNICATION

Simplifying ovulation induction for surrogacy in women with Mayer–Rokitansky–Kuster–Hauser syndrome

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A simple approach for ovulation induction in women with Mayer–Rokitansky–Kuster–Hauser Syndrome (MRKH-S) during in-vitro fertilization (IVF)/freezing/surrogacy cycles was evaluated. Weekly progesterone plasma concentrations were measured in order to accurately establish the luteal phase in MRKH-S women. When a rising titre was detected, a gonadotrophin-releasing hormone analogue (GnRHa) was administered as part of a long protocol. Two weeks later human menopausal gonadotrophin (HMG) therapy was started. Ten treatment cycles in four women with MRKH-S were carried out. In all cases, three or less progesterone estimations were needed. Three of the four women are now, through surrogacy, genetic mothers; one of them has two children. We concluded that weekly determination of progesterone plasma concentration is a convenient, efficient and inexpensive simple approach to identify the luteal phase, and therefore suitable to the start of a GnRHa/HMG protocol in MRKH-S women enrolled in an assisted reproduction technology programme.

Key words: ART/Mayer–Rokitansky–Kuster–Hauser/ovulation induction

Introduction

Mayer–Rokitansky–Kuster–Hauser syndrome (MRKH-S) is a relatively common cause of primary amenorrhoea (Griffin et al., 1976). This syndrome of Mullerian agenesis includes an absent or hypoplastic vagina. The uterus may be normal, but often is rudimentary. While creation of a neo-vagina facilitates normal sexual intercourse, infertility is the rule, except for rare cases with an intact uterus. Since ovarian activity is completely preserved, it is possible to offer motherhood through a combination of in-vitro fertilization (IVF) and surrogacy. Ovulation induction should be similar to any other case, except for the fact that lack of menstruation due to outflow track obstruction precludes the identification of the menstrual day. Accordingly, it is mandatory to identify the follicular phase and time of induction. The aim of the study was to evaluate a simple approach to identify a starting day of ovulation induction as part of a surrogacy protocol.

Materials and methods

Between 1992 and 1996, four women with MRKH-S underwent 10 treatment cycles in our IVF surrogacy programme; all were included in this study. The mean age of the patients was 26 years. No male factor infertility was noted. The diagnosis was made in all cases during puberty. Three patients underwent surgical procedures to create a neo-vagina after puberty, before marriage, and according to Frank (1938), one used progressive dilators of the vagina.

IVF studies included routine hormonal, transvaginal ovarian investigations and spermogram. For the stimulation protocol, we developed this simplified method, since the lack of menstruation precluded simple identification of the follicular phase. We therefore planned to give gonadotrophin-releasing hormone analogue (GnRHa) during the luteal phase for 2 weeks, and then to start with human menopausal gonadotrophin (HMG) 2–3 ampoules per day. The patients were instructed to measure progesterone only, once weekly. Once the progesterone concentration was found to be $>6$ nmol/l, the MRKH-S women were considered to be in the luteal phase. At that stage we treated them with long-acting GnRHa (Decapeptyl depot 3.75 mg; Ferring, Malmo, Sweden) as part of a long protocol. Two weeks later down-regulation was ascertained and HMG, 2–3 ampoules per day, was initiated. Human chorionic gonadotrophin (HCG) administration and transvaginal ovum collection were performed routinely (Ben-Rafael et al., 1995). Embryos were frozen at the two pronuclear (2PN) stage to be transferred later to a surrogate mother.

Results

Ten treatment cycles in four women with MRKH-S were carried out utilizing the aforementioned approach. In all cases, three or fewer estimations of progesterone were needed in order to detect the luteal phase. Inconvenient and expensive repeated transabdominal ultrasound examinations in this initial pre-treatment phase were avoided. Ovulation induction was successful in all women utilizing the long protocol. Ovum collection through the neo-vagina posed no real problem. The number of eggs collected was 8–24 (mean 14.6) and the fertilization rate was 71%. Three of the four women are now genetic mothers through surrogacy; one of them has two children.

Discussion

MRKH-S is a common diagnosis in women with primary amenorrhoea and absence of a vagina. These women are
potentially fertile through surrogacy, since their ovarian function is usually intact. Furthermore, they are relatively young when they apply for treatment and hence are good responders. Surrogacy is a well-established procedure in certain countries and the medical procedure relies on regular IVF protocols. Egarter and Huber (1988) were the first to describe attempts at stimulation of a patient with MRKH-S. They used a clomiphene-citrate/HMG protocol with the subsequent laparoscopic retrieval of two oocytes which were successfully fertilized and then frozen for future surrogacy. Batzer et al. (1992) later provided an excellent review of the medical, legal and ethical issues regarding the genetic offspring in MRKH-S patients.

While Egarter and Huber (1988) did not provide any details on the timing of the ovulation induction protocol, Batzer et al. (1992) described the use of oral contraceptives in the MRKH-S patients. This method was used in order to synchronize the menstrual cycles of the donor and recipient, so that cessation of oral contraceptives in the donor coincides with cycle day 1 of the recipients. They mentioned the alternative of using GnRHa, without providing further details, or a method to detect the menstrual cycle phase.

Since frequent, repetitive plasma hormonal testing would be rather cumbersome, we offered this simple approach of weekly determinations of plasma progesterone concentration. We encountered no real problems, and in fact the success of IVF/freezing/surrogate treatment was high (four deliveries in three women out of 10 cycles). For clinical convenience, we devised this protocol that, by simple means, made it possible to identify the luteal phase, down-regulate for 2 weeks to reach the follicular phase, and then stimulate with HMG, even without being aware of the day of menstruation.

We found that weekly determinations of plasma progesterone concentration are a convenient, efficient and inexpensive means of achieving pregnancy in MRKH-S women enrolled in an assisted reproductive technology programme.

References

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