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Case Report

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Two Successful Pregnancies in A Woman with Marked Diminished Ovarian Reserve-One with Regular Menses and One in Overt Menopause

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ABSTRACT

An FSH receptor up- regulation technique has been used to induce ovulation with successful achievement of healthy babies even in women with hypergonadotropic amenorrhea with estrogen deficiency. For many years the same technique has been used in women who were not in menopause but still having menses. One had diminished oocyte reserve (DOR). A 32-yearold woman with 2 1/2 years of infertility was advised to consider donor eggs by her first consult with an infertility specialist because she had mild DOR even though basal body temperature charts indicated possibly achieving pregnancies naturally but having early miscarriages. Her first pregnancy with our group only required progesterone supplementation. Interestingly, she went into complete ovarian failure during that pregnancy. Her second successful pregnancy was achieved by restoring follicular sensitivity by restoring FSH receptors in the granulosa theca cells with P supplementation once a mature dominant follicle was achieved without any addition of exogenous gonadotropins. The case illustrates the importance of early monitoring of hormone levels shortly after delivery if a woman desires another baby since amenorrhea is common post-delivery for several months. The treating physician may not be alarmed to evaluate ovarian reserve status just because of amenorrhea for a period of time. Both babies were healthy with no evidence of aneuploidy.

Keywords: Diminished Ovarian Reserve, Premature Ovarian Failure, Ethinyl Estradiol, FSH Receptor Up-Regulation

Introduction

Women with diminished ovarian (DOR), which is sometimes called premature ovarian insufficiency (POI), have been shown to be able to have three live babies over an eight-year time span both with in vitro fertilization embryo transfer and natural pregnancies [1,2]. The precise technique for treatment depends on the degree of DOR and the serum estradiol (E2) and is called the FSH receptor up regulation technique [3-5]. The technique in the mildest case is merely to add luteal phase P support if the woman is already making a mature dominant follicle with adequate length to the follicular phase or to merely lengthen the follicular phase by ethinyl estradiol (EE) to lower the serum FSH to decrease the speed of follicular development or to adding a boost of gonadotropins if the FSH is low enough (adding it when the serum FSH is still elevated down regulate FSH receptors) or adding a gonadotropin releasing hormone antagonist if there is premature luteinization to slow down progression. If normal levels of serum FSH have been restored, or if there is a desire to try to develop more than1 dominant follicle, a small dosage of FSH (25-150 mIU) can be added earlier in the follicular phase [3-8].

A case is described where a woman with regular menses, but mild DOR, achieved a live delivery merely by adding P. However, she went into overt menopause sometimes during her pregnancy and required restoration of down-regulated FSH receptors with EE to achieve her second baby.

Case Report

A 32-year-old woman consulted another reproductive endocrine infertility group because of 2 1/2 years of primary infertility. She had regular cycles of usually 28 to 30 days but sometimes they could be as long as 34 days. Her serum FSH obtained on day three of her menstrual cycle was 22 mIU/ml with a serum E2 of 27pg/ml. Her anti-mullerian hormone level was 0.65ng/ml. Surprisingly, the REI specialist told her that with DOR the only option was to use donor oocytes. She sought a second opinion from our group.

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Prior to her visit with the first REI, she had brought with her a year's worth of basal body temperature charts (BBTs). We advised her that some of the longer cycles, e.g., 34 days showed a longer luteal phase, thus suggesting that = she may be conceiving, but having early pregnancy losses. She was seen on day 28 of her cycle and her BBT was elevated for 13 days. Her beta human chorionic gonadotropin (hCG) level was 35mIU/ml and her serum P was 9.7ng/nl. We prescribed progesterone vaginal compounded, suppositories 400 mg twice daily and 100 mg intramuscular (IM) P. Eventually, we were able to wean her off the 1MP but continued the progesterone vaginal suppositories until her full-term delivery of a healthy girl.

During that pregnancy, she stated that her goal was to have two children, but, if possible, she would like to have them 2 to 3 years apart. We advised her of the two patients that had three babies eight years apart. Nevertheless, we advised her that we would reevaluate her egg reserve three months after delivery. Despite nursing her baby, her serum FSH was 93 mIU/ml with a serum E2 <15pg/ml. Her serum AMH level was 0.03ng/ml.

One month later, her serum E2 remained < 5pg/nl and her serum FSH 109 mIU/ml. She decided that she would try immediately to conceive. Her serum. E2 began to rise on day 22 of EE 20 micrograms per day once her serum FSH was reduced to 37 mIU/ml. After 30 days of EE her serum E2 was 272pg/ml with a serum FSH of 18.5mIU/ml.

She was not given any gonadotropin boost because her serum FSH did not approach the level of 12-14mIU/ml when we may consider a boost of exogenous FSH. She conceived that cycle and delivered another healthy baby girl at 37 weeks. Again, the vaginal P was maintained until delivery. We frequently stopped the P after the first trimester, but give the patient the option of continuing to term. She chose to continue to term both times.

Discussion

The patient had no symptoms of the increased cellular permeability syndrome, e.g., dysmenorrhea, or pelvic pain of any kind, or gastrointestinal, dermatologic, musculoskeletal, or neurologic symptoms that can lead to DOR or premature ovarian failure (POF) by inflammatory damage [9]. We advised her that just having DOR or POF can be an indicator that she could benefit from the addition of dopaminergic drugs.

However, in the first pregnancy, she conceived on her own, but just used the progesterone supplementation to prevent a miscarriage [10-12]. She stated that she would consider a dopamine agonist if she was not pregnant in 3 to 4 months. Thus, both pregnancies were achieved with dopamine agonists.

This case illustrates that the achievement of a pregnancy with the E2 and P suppressing FSH and LH and the immunological changes during pregnancy do not protect against accelerated egg loss.

She was given the option of IVF with cryopreservation of embryo for a future pregnancy but for financial reasons, and because having two children so close together was not a tremendous hardship, she elected to try to get pregnant naturally right away [13,14]. This case emphasizes the fact that even with POF pregnancy can be achieved naturally without the use of IVF [15-17].

The initial REI had quoted the statistics of a publication in 2005 in the journal. Fertility and Sterility finding no live deliveries in women having normal appearing embryos transferred with IVF – ET if the woman had serum FSH levels over 18 three times [18]. We explained that based on our successes, even without IVF-ET, we think the failure reported by this world-renowned REI center was probably related to stimulating with too much FSH thus raising serum levels even higher and possibly down regulating a key FSH receptor needed to produce an enzyme or cytokinin need it for successful implantation [4].

The advantage of using ethinyl estradiol is that it is potent enough to suppress serum FSH with a 20-µg pill daily and yet not contribute to the serum E2 levels thus allowing accurate determination of follicular maturation [19].

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