

## **SPONTANEOUS OVULATION AND SUCCESSFUL PREGNANCY DESPITE BILATERAL STREAKED OVARIES**

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*Secondary ovarian failure has been estimated to occur in approximately 1% of women under age 40. Many regimens have been used to promote conception in those patients. Reports of pregnancies after treatment with estrogen, clomiphene citrate, hMG and/or a GnRH analog have been published. Greater success had been associated with donor oocytes via in vitro fertilization (IVF) or gamete intrafallopian transfer (GIFT). Only one case has been reported of spontaneous ovulation and pregnancy in a patient with streaked gonads. The case described herein is of a 33 year-old amenorrheic patient who had persistently elevated sera FSH levels and laparoscopic confirmation of bilateral streaked ovaries. The patient conceived without any treatment and delivered a healthy term baby. This case demonstrates that even if very few follicles are present, sporadic spontaneous recruitment may occur even without estrogen replacement. The possibility may still exist that estrogen therapy can further the likelihood of successful ovulation in this group.*

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## INTRODUCTION

The treatment of ovarian failure with the aim of establishing a pregnancy has received a great deal of interest recently, especially since the publication by Lutjen of fertilization of donor oocytes with subsequent embryo transfer.<sup>1</sup> There have been several studies demonstrating very high pregnancy rates with donor oocyte programs.<sup>2,3</sup> In fact, there is evidence that these ovarian failure patients have a higher pregnancy rate than eugonadotropic women.<sup>4,5</sup>

There have also been several anecdotal case reports of ovulation induction and subsequent pregnancy in women with hypergonadotropic amenorrhea.<sup>6-11</sup> However, success rates in these women have been quite low. In a series of 100 consecutive cases, a take home baby rate of 8% was reported, with a live birth per treatment cycle of only 2.6%.<sup>12</sup>

Despite the data demonstrating a far greater likelihood of success with donor oocyte versus natural oocyte fertilization, many women prefer to at least try with their own oocytes first. Most reported pregnancies have resulted from some type of therapy, mainly hormone replacement therapy.<sup>13-15</sup> Pregnancies occurring in untreated women are rare. One such case is presented herein.

## MATERIALS AND METHODS

**Source** - 33 year-old woman with a 4 year history of amenorrhea with estrogen deficiency as evidenced by her failure to have withdrawal menses following medroxyprogesterone acetate 10 mg for 10 days. By history her gonadotropins were elevated, but the exact levels of serum LH and FSH were not known

to our center. Although measurement of serum FSH was 69 mIU/mL (nl 3.5 to 16.9) with a serum estradiol ( $E_2$ ) <20 pg/mL, the LH was normal at 14 mIU/mL (nl 4.9 to 25.1) on initial testing by our group. The assays included were FSH by Chemiluminescence (Amerlite Diagnostics, Ltd., Buckinghamshire, England), LH by double antibody radioimmunoassay (Amersham Corp, Arlington Heights, CA), and estradiol by solid phase radioimmunoassay (Diagnostic Products Corporation, Los Angeles, CA). A laparoscopy confirmed the presence of bilateral streaked gonads.

### **Suggested Treatment**

Estrogen in the form of ethinyl estradiol was recommended but, because of a history of endometriosis and fear the estrogen would stimulate a return of that condition, the patient refused. Leuprolide was also offered. The patient, however, had previously experienced untoward side effects from the drug when it was used to treat endometriosis, and she declined the leuprolide treatment as well.

### **Actual Treatment**

The patient was stimulated with human menopausal gonadotropins (hMG) but despite 10 ampules (75IU each), she failed to raise her serum  $E_2$  level above 20pg/mL. Of interest was the fact that after discontinuing hMG, menses resumed and continued approximately every 21 days. She returned after nine months for evaluation of hormone levels and was still found to be estrogen deficient with even higher gonadotropins (FSH = 124 mIU/mL and LH now increased to 83 mIU/mL). Her thyroid profile at that time was normal; T4 was 8.6 (nl 5.0-12.0ug/dL), TBG was 30ug/ml (nl 12-46), T3RIA was 97ng/mL (nl 52-160) and TSH was 2.1uIU/mL (nl 0.35-7.0). Her morning serum cortisol of 10.6ug/nL was also normal.

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## RESULTS

### Description of Pregnancy

The patient's menses stopped again and 13 months later she had a beta human chorionic gonadotropin (hCG) level obtained which was surprisingly positive with a level of 55,435mIU/mL. A sonogram at that time confirmed that she was 11 weeks pregnant. Following an uncomplicated pregnancy, she delivered a healthy girl at 42 weeks.

### Hormonal Events Post-delivery

Amenorrhea persisted after delivery. A repeat test for gonadotropins 9 months post-delivery found elevated levels of FSH (75.9mIU/mL), and LH (105mIU/mL), but the E<sub>2</sub> level reached 117pg/mL. Her peak E<sub>2</sub> reached 138 and a follicle of 18.6mm was sonographically attained. This follicle subsequently collapsed consistent with ovulation. Prior to progesterone (P) supplementation, her serum (P) attained a level of 4.2ng/dL, but she failed to conceive.

## DISCUSSION

The incidence of women under age 40 having secondary ovarian failure has been estimated at approximately 1%.<sup>16</sup> Two basic mechanisms may explain the phenomena of premature ovarian failure: 1) a paucity of follicles and 2) autoimmune folliculitis.<sup>17,18</sup> The latter would be a condition more likely to be associated with spontaneous resumption of menses, since a normal number of follicles exist; a spontaneous remission of the immunologic conditions would then allow the immature oocyte to progress to maturity without immunologic destruction.

Only once before has a case been described providing clear-cut evidence of streaked gonads with subsequent ovulation and pregnancy<sup>19</sup> but, in this case, high dose estrogen and hMG were used. Previous failure to stimulate with hmG, but subsequent ovulation and pregnancy following estrogen and hMG, has been reported.<sup>9</sup> One theory is that estrogen sensitizes the follicles by synergizing with FSH to increase the number of FSH receptors.<sup>20,21</sup>

The case described herein demonstrates that when very few follicles exist, but at least some are still present, spontaneous recruitment may sporadically occur even without estrogen replacement. A prospective study is needed to determine if estrogen therapy increases the likelihood of recruitment of follicles despite hypergonadotropic hypogonadism. The majority of women with this diagnosis receive estrogen replacement therapy for health reasons; pregnancies which occur while taking this therapy cannot necessarily be considered a result of that therapy.

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