

Amenorrhea in an ovulatory woman despite a normal uterine cavity: Case report

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A 35-year-old nulliparous woman came to us for treatment of amenorrhea. Evaluation demonstrated normal ovulation with appropriate results of sequential endometrial biopsies during the luteal phase. The only abnormality found was an elevated serum level of follicle-stimulating hormone in the early follicular phase, and it is hypothesized that this somehow leads to atrophy of the endometrium without shedding. (AM J OBSTET GYNECOL 1989;160:598-9.)

Key words: Amenorrhea, follicle-stimulating hormone, endometrium

Amenorrhea despite proved ovulation is usually attributed to Asherman's syndrome. A case is presented in which ovulation and normal endometrium were found by serial endometrial biopsies, yet there was no evidence of intrauterine synechiae demonstrated by both hysterosalpingogram and hysteroscopy.

Case report

A 35-year-old nulliparous woman sought consultation concerning her potential ability to achieve a pregnancy. She gave a history of having a last menstrual period 4 years before. During the past year she noticed three episodes of spotting lasting no more than 2 hours. She denied ever having curettage and there was nothing in her history to suggest a previous endometritis.

A diagnosis of "premature ovarian failure" had been previously made, but she wanted to discuss the likelihood that ovulation could be induced despite this diagnosis. This would influence her husband's decision to have microsurgical reanastomosis of a previously ligated vas deferens.

Serum hormonal levels were determined to confirm the previous diagnosis. Though the level of follicle-stimulating hormone (FSH) was slightly elevated at 32 mIU/ml (normal 0 to 20), the level of luteinizing hormone was in the high normal range at 32 mIU (normal 0 to 38), but of great interest was that the serum estradiol level was 230 pg/ml (a good periovulatory level) and the serum progesterone level was 0.6 ng/ml. Other hormonal levels were normal, including the dehydroepiandrosterone sulfate level (137 ng/ml), prolactin (7 ng/ml), testosterone (17 ng/dl), thyroxine (6.9 ng/ml), triiodothyronine uptake (27%), and thyroid-

stimulating hormone (1.2 mIU/ml). The hematocrit was 36%, which was slightly low and a little surprising in view of the amenorrhea, but may have been related to poor dietary habits. Despite the good serum estradiol level the patient did not have a withdrawal menstrual period even with the administration of medroxyprogesterone acetate 10 mg for 10 days. She also did not have a withdrawal menstrual period despite receiving conjugated estrogen 5 mg for 25 days plus medroxyprogesterone acetate for the last 13 days.

She was given clomiphene citrate 50 mg for 5 days, and 5 days after the pills were discontinued, the serum estradiol level was measured at 319 pg/ml with the serum progesterone level at 1.0 ng/ml; the luteinizing hormone level was 37 mIU/ml. A follicle with an average diameter of 19 mm was seen in the left ovary. The serum estradiol level increased to 500 pg/ml 7 days after clomiphene administration was stopped and the follicle diameter increased to 24.3 mm. The serum progesterone level was 1.1 ng/ml and the level of luteinizing hormone 29 mIU. The serum progesterone level increased to 19.2 ng/ml 14 days after clomiphene administration was discontinued. However, she did not have a menstrual period and the human chorionic gonadotropin β subunit level was negative.

A laparoscopy was performed and the findings normal except for two implants of endometriosis right of the midline along the vesicouterine fold of peritoneum. Multiple corpora lutea were seen on the surface of the left ovary and a recent corpus luteum was seen on the proximal pole of the left ovary. Hysteroscopy did not reveal any significant intrauterine synechiae. This was performed in the early follicular phase; the endometrium appeared atrophic and no tissue could be obtained.

A hysterosalpingogram was performed with instillation of Conray water soluble contrast material 20 ml into the uterine cavity. No adhesions were visualized and the cavity was a normal size. The patient was carefully evaluated during one cycle, and the results are seen in Table I. The patient had documented evaluated

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Table I. Detailed hormonal evaluation of one cycle

| | Day of ovulation | Days past ovulation | | | |
|------------------------------|------------------|---------------------|------|--------|-----|
| | 0 | 2 | 7 | 14 | 16 |
| Estradiol (pg/ml) | 285 | | 189 | 112 | <20 |
| Progesterone (ng/ml) | 1.9 | | 30.5 | 4.1 | 1.0 |
| FSH (mIU/ml) | 20 | | 9 | | 73 |
| Luteinizing hormone (mIU/ml) | 28 | | 14 | | 30 |
| Endometrial biopsy results* | | +2 | +7-8 | +11-12 | |

Biopsy dated according to Noyes et al.⁴

*Results of endometrial biopsy indicate days past ovulation.

FSH levels in the follicular phase in three other cycles. She was examined at the time of expected menses and the absence of blood was confirmed.

Comment

This case depicts two clinical events that are extremely difficult to explain, and one has to wonder if these two events are related to each other or are independent. We are not aware of a known mechanism that can account for normal ovulation, normal endometrial biopsy results, the absence of uterine synechiae or obstruction, and yet no menses. Some animals, such as rabbits, sheep, and hamsters have hypertrophy and degeneration of uterine luminal epithelium in response to estrogen and progestins; however they do not menstruate but undergo a process of cell destruction by apoptosis.¹ Those animals lack the spiral arterioles that are responsible for the menstrual flow in primates.

The other unexplainable phenomenon is the fact that the FSH level in this patient rises to menopausal levels in the early follicular phase. This was the reason for the previous false diagnosis of premature ovarian failure by her previous physicians. Somehow it seems logical that these two rare events are somehow linked. Perhaps there is some defect in inhibin that leads to a rise in the level of FSH when the estradiol levels are low but that does not affect luteinizing hormone, and in which as the estradiol levels rise above a certain point, the FSH is suppressed via negative feedback into the normal range.

McLennan and Rydell² found that the extent of endometrial tissue shedding varies widely from one uterus to another and is less extensive than many believe it to be. They concluded that in most cases an

appreciable fraction of the stratum spongiosum actually disintegrates but endometrial tissue superficial to the basal layer remains in situ at the end of menstruation. Bartelmez³ concluded that the marked reduction in the thickness of the endometrium is primarily due to loss of fluid and the resulting collapse of the spongy layer. Thus the possibility exists that this patient tends to form a compact stratum functionale without any endometrial tissue shedding. Because amenorrhea despite proved ovulation with normal luteal phase endometrial samplings and a normal uterine cavity is a rare event (we could not find a previous documented case) and because normal ovulation despite postmenopausal follicular phase FSH levels is certainly unusual, one has to wonder whether somehow these two conditions are interrelated.

Since prostaglandin suppression has been associated with decreasing excessive menstrual bleeding, the possibility exists that the patient has some prostaglandin abnormality. The patient denies taking prostaglandin suppressor drugs except for an occasional aspirin.

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