

Pregnancy in premature ovarian failure after therapy with oral contraceptives despite resistance to previous human menopausal gonadotropin therapy

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We report the case of a 35-year-old woman with premature ovarian failure that was documented at 29 years of age, who wanted to conceive. Although she failed to respond to high doses of menotropin therapy, she ovulated and conceived after she took an oral contraceptive. The oral contraceptive was used to reduce the elevated level of gonadotropins in an effort to restore receptors to the luteinizing hormone and follicle-stimulating hormone, which theoretically may have been down-regulated. (AM J OBSTET GYNECOL 1989;160:114-5.)

Key words: Ovarian failure, oral contraceptive, pregnancy

There have been two cases reported in which women with premature ovarian failure (hypergonadotropic hypogonadism) that occurred before they were 40 years of age conceived while taking oral contraceptives.^{1, 2} Neither of these women had tried to conceive, but pregnancy occurred spontaneously while they were taking oral contraceptives. Our case involves a woman with premature ovarian failure and no increase in serum estradiol levels despite a high dose of human menopausal gonadotropins (hMG) but who was able to conceive while taking an oral contraceptive.

Case report

The patient was seen at age 31 and had a history of 1½ years of amenorrhea. An evaluation 1 year earlier had shown hypergonadotropic amenorrhea (luteinizing hormone [LH] increased 125 mIU/ml and the follicle-stimulating hormone [FSH] increased to 148 mIU/ml). Her previous consultant had told her no therapy could help her achieve a second pregnancy; she had an 8-year-old child at that time. However, she sought another opinion.

The gonadotropin measurements were repeated and the serum FSH was increased to 156.6 mIU/ml, the LH was 104 mIU/ml, and the serum estradiol level was <20 ng/ml.

The patient was given 1200 IU of hMG over an 8-day period, but it failed to raise the serum estradiol

level above 20 ng/ml. She elected to discontinue the treatment.

Two years later, at the age of 33, she decided to resume therapy. However, a 5 cm mass was felt in the left adnexa during a pelvic examination. Pelvic ultrasonography confirmed a 50 × 47 × 43 mm multicystic area composed of 10 to 12 cysts that ranged from 15 to 19 mm each and extended under the uterus. She still had amenorrhea and the FSH level was 240 mIU/ml, the LH level was 133 mIU/ml, and the estradiol level was <20 pg/ml.

The patient was to be treated with a high-dose estrogen-hMG technique to induce ovulation.³ However, because of the ovarian cyst, the decision was made to suppress the gonadotropins by means of an oral contraceptive (35 µg ethinyl estradiol, 1 mg norethindrone) to determine whether the cyst could be reduced. The patient was instructed to return in 1 month to have the cyst evaluated, at which time inauguration of the high-dose estrogen-hMG technique would be considered. However, she did not return until 3 months later.

Repeat ultrasonography showed the cystic ovary reduced to normal size, with one cyst 25 mm and one 16 mm in diameter. She demonstrated a single intrauterine fetus with a sac of 29 to 30 mm, consistent with 7.8 weeks' gestation. There was good decidual reaction, shape, and position. The crown-rump length measured 15 to 16 mm, consistent with 7.6 to 8 weeks' gestation. The patient stated that the last menstrual period was after cessation of the first cycle of the oral contraceptive.

Comment

One possible explanation of this pregnancy is that the elevated gonadotropin levels caused a "down-regulation" of FSH and LH receptors on the granulosa-theca cells. The oral contraceptive caused suppression

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of the gonadotropins to the normal range, which allowed restoration of receptors and response to the endogenous gonadotropins.

This case, in contrast to the two previously reported cases, demonstrated the inability to respond to exogenous gonadotropins, and yet the patient ovulated spontaneously after one cycle of an oral contraceptive. This further supports the proposed mechanism of reversing hypergonadotropic hypogonadism by restoring receptors to LH and FSH by first suppressing elevated gonadotropins. The case suggests that before the initiation of the expensive high-dose estrogen-hMG tech-

nique,³ the patient might try one cycle of oral contraceptive therapy, after which the succeeding cycle would be evaluated with regard to possible rebound spontaneous ovulation.

REFERENCES

1. Muram D, Jolly EE. Pregnancy and gonadal dysgenesis. *Obstet Gynecol* 1982;3:87.
2. Alper MD, Jolly EE, Garner PR. Pregnancies after premature ovarian failure. *Obstet Gynecol* 1986;67:595.
3. Check JH, Chase JS. Ovulation induction in hypergonadotropic amenorrhea with estrogen and human menopausal gonadotropin therapy. *Fertil Steril* 1984;42:919.