

Ovulation induction and pregnancy with an estrogen-gonadotropin stimulation technique in a menopausal woman with marked hypoplastic ovaries

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A case is described of a woman with ovarian failure and documented atrophic ovaries in whom ovulation was achieved with the use of high-dose estrogen and human menopausal gonadotropins. The proposed mechanism involves a reduction in the elevated gonadotropins, which restored an adequate number of receptors. Thus sensitivity to exogenous menotropins was reestablished. (AM J OBSTET GYNECOL 1989;160:405-6.)

Key words: Ovulation, menopausal hypoplastic ovaries

Induction of ovulation in women with ovarian failure has been described as the stimulation of remaining ovarian follicles with gonadotropin therapy after the elevated gonadotropins have been suppressed into the normal range by either exogenous estrogen therapy¹ or by leuprolide acetate.² The hypothesized mechanism by which follicular maturation occurred in patients who previously had failed to respond to human menopausal gonadotropins (hMG) alone, involved the renewal of sensitivity to gonadotropins of some of the remaining follicles by the restoration of gonadotropin-receptor concentration. This had been down-regulated by the previously elevated levels of luteinizing hormone (LH) and of follicle-stimulating hormone (FSH).

However, in none of these cases in which gonadotropin suppression preceded hMG stimulation was there any morphologic documentation of a paucity of ovarian follicles. The possibility exists that there was an inhibitor present (e.g., antibodies to the receptors) that prevented follicular stimulation spontaneously or to exogenous gonadotropins. Thus, after spontaneous remission of the problem, the normal cohort of follicles would respond appropriately to LH and FSH with resultant ovulation.

A case is reported in which ovulation and subsequent pregnancy occurred in a menopausal woman after gonadotropin suppression with ethinyl estradiol and stimulation with hMG. However, in this case there was definite morphologic documentation of a marked diminution of ovarian tissue.

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Case report

A 39-year-old woman with secondary infertility was first seen with a diagnosis of ovarian failure. Her menarche occurred at age 10 years and she had regular menses up to age 32 years when oligomenorrhea developed. Vasomotor symptoms started at age 30 years. Her last spontaneous menstrual period occurred at age 38 years, and 100 mg progesterone in oil administered intramuscularly was unable to induce menses.

Serum LH and FSH at the time of initial examination were elevated into the menopausal range at 112 and 124 mIU/ml, respectively, and the serum estradiol level was 12 pg/ml. Serum levels measured 3 weeks later showed similar elevations in gonadotropins (LH = 85 mIU/ml, FSH = 96 mIU/ml, and serum estradiol = 8 pg/ml). The levels of serum thyroxine, triiodothyronine, triiodothyronine resin uptake, thyroid-stimulating hormone, 8 AM cortisol, antinuclear antibody, serum calcium, and fasting serum glucose were normal, as was the complete blood count. Chromosome analysis showed 46,XX.

A laparoscopy revealed a hypoplastic yellowish left ovary approximately 20 mm × 16 mm × 16 mm, but no right ovary was identified. Neither adhesions or endometriosis were noted, and the fallopian tubes and the uterus appeared normal.

Six months before her initial visit she had been treated with 3000 IU hMG, which failed to raise the serum estradiol level above 20 pg/ml. The next month the serum estradiol level did not increase above 20 pg/ml despite treatment with 3600 IU hMG.

The patient was started on 50 µg ethinyl estradiol daily for 2 weeks and 150 IU hMG daily for 4 days. The hMG was increased to 225 IU thereafter. She ovulated that cycle and formed one mature follicle that averaged 18.6 mm in diameter as measured by means of ultrasonography. The serum estradiol level reached 292 pg/ml. Release of the ovum was demonstrated by shrinkage of the follicle to 11 mm as measured by means of ultrasonography. She was placed on 25 mg

of progesterone vaginal suppositories twice daily and a midluteal-phase serum progesterone level was measured at 17.6 ng/ml. An endometrial biopsy specimen taken 13 days from ovulation was 4 days out of phase. An endometrial biopsy specimen taken 13 days from her second induced ovulation after 75 mg/day progesterone supplementation was in phase. A total of 3000 IU hMG was required the first cycle and 4800 IU hMG the next cycle. The maximum amount per day was 225 IU hMG.

The patient ovulated the next five consecutive cycles with the use of the same technique and averaged 2375 IU hMG per cycle. She skipped one cycle and ovulated again after the administration of 3400 IU hMG. She conceived in this cycle.

She was delivered of her infant by cesarean section at 37 weeks' gestation. At that time the right ovary was identified as a streaked gonad and the left ovary appeared even more hypoplastic than before and was estimated to have an average diameter of 12 to 15 mm.

Comment

The morphologic appearance of the ovaries in the case described supports the contention that, in this pa-

tient, ovarian failure was related to a paucity of follicles rather than to a normal number of follicles that were resistant to gonadotropin stimulation. Attempts failed to stimulate even a mild elevation in the serum estradiol levels with hMG alone in two cycles versus seven consecutive ovulatory cycles in which ethinyl estradiol was used to suppress the elevated gonadotropins into the normal range before the start of hMG therapy. This is consistent with the concept that the few remaining follicles had been resistant to gonadotropin stimulation because of down-regulation of the gonadotropin receptors.¹

REFERENCES

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