

## Ovulation and successful pregnancy in a woman with ovarian failure after hypophysectomy and gonadotropin therapy

Jerome H. Check, MD

Camden, New Jersey

A 38-year-old woman ovulated and conceived after administration of human menopausal gonadotropins despite a previous diagnosis of ovarian failure at age 18. Possible explanations include restoration of down-regulated gonadotropin receptors by development of a prolactinoma, spontaneous remission of autoimmune oophoritis, or prior tumor secretion of biologically inert gonadotropins. (AM J OBSTET GYNECOL 1990;162:775-6.)

**Key words:** Ovarian failure, prolactinoma, pregnancy, human menopausal gonadotropins, hypophysectomy

Ovulation induction has been achieved in some women with ovarian failure by first suppressing elevated gonadotropin levels with high-dose estrogen (ethinyl estradiol<sup>1</sup>) or with gonadotropin-releasing hormone agonists (leuprolide acetate<sup>2</sup>) followed by stimulation with human menopausal gonadotropins (hMG). Pregnancies also have been recorded.

A case is described of another viable pregnancy recorded in a woman with ovarian failure. This patient also responded to hMG stimulation after gonadotropin suppression; but in this case reduction of the high luteinizing-hormone (LH) and follicle-stimulating hormone (FSH) levels was attained after hypophysectomy for pituitary macroadenoma.

*From the Division of Reproductive Endocrinology and Infertility, Department of Obstetrics and Gynecology, Cooper Hospital/University Medical Center, Robert Wood Johnson Medical School at Camden, The University of Medicine and Dentistry of New Jersey. Received for publication August 28, 1989; accepted September 13, 1989.*

*Reprint requests: Jerome H. Check, MD, 1015 Chestnut St., Suite 1020, Philadelphia, PA 19017.  
6/1/16659*

### Case report

A 35-year-old woman was seen for evaluation of secondary amenorrhea. Menarche occurred at age 13, but at age 18 oligomenorrhea developed, followed by amenorrhea. She was evaluated at a university hospital and was told that the urinary gonadotropin levels were elevated, suggesting premature menopause (records not available), and that she would never be able to conceive. After marriage, she was reevaluated because of amenorrhea and infertility at age 27 and was once again informed that, on the basis of increased serum LH (92 mIU/ml) and FSH (78 mIU/ml) levels, ovulation and subsequent pregnancy would be exceedingly rare. During both evaluations the patient failed to have menses after being given medroxyprogesterone acetate 10 mg for 10 days.

Laboratory studies demonstrated a serum estradiol level of 5 pg/ml and LH and FSH values <1.0 mIU/ml. The serum prolactin level was very elevated at 975 ng/ml. Thyroid and cortisol levels were normal.

Computerized axial tomography revealed a large pituitary mass with suprasellar extension into both the sphenoid sinus and left middle fossa. After bromocriptine therapy, the tumor shrank to 50% of its original

size and a successful transsphenoidal hypophysectomy was performed.

Although serum prolactin levels remained between 400 and 600 ng/ml (while serum LH and FSH values remained low), despite therapy with bromocriptine 5 mg daily, no growth of the prolactinoma was noted. She requested attempts for ovulation induction to try to achieve a pregnancy at age 37 despite the knowledge that the estrogen of pregnancy could enhance tumor growth.

She was treated with hMG and ovulated in 6 of her first nine cycles, averaging 3950 IU of hMG, and serum estradiol levels ranging from 220 to 1055 pg/ml were attained during her ovulatory cycles. She conceived in her ninth and tenth hMG-treated cycles but aborted during the first trimester after fetal viability was shown by sonography 5 weeks after conception in both instances.

A third conception was recorded on her second hMG cycle after the previous abortion. She was treated throughout the pregnancy with supplemental progesterone and was delivered prematurely (at 31 weeks' gestation) of a male infant who is doing well 1 month after delivery.

#### Comment

We believe the 20-year interval, from initial diagnosis of ovarian failure to pregnancy, to be the longest one reported, unfortunately without an anatomic diagnosis (laparoscopy and ovarian biopsy were not thought to be clinically warranted). There are at least two possible explanations for the events that occurred in this patient.

The first possibility is that the tumor began as a gonadotropin- and prolactin-secreting lesion but the

LH and FSH produced were biologically inert. Eventually, the tumor enlarged, causing necrosis of the gonadotropin cells, and became a pure prolactinoma. Thus, if this model is correct, perhaps this woman might have responded to hMG therapy at age 27, when serum LH and FSH levels were still elevated. However, against this hypothesis is the rarity of gonadotropin-secreting tumors; furthermore, to our knowledge there has never been a report of the conversion of these tumors to a macroadenoma secreting exclusively prolactin.

Another possible explanation for these clinical events is that the ovarian damaging process ceased at age 18, but the resulting elevation of gonadotropin levels resulted in down-regulation of gonadotropin receptors, thus inhibiting response to endogenous gonadotropins. Restoration of receptors would theoretically occur with the suppression of LH and FSH by the hyperprolactinemia and subsequent hypophysectomy.

Finally, a third hypothesis is that the patient went into spontaneous remission of autoimmune oophoritis (no damage to ovarian tissue occurs) but failed to spontaneously ovulate because of the fortuitous development of the prolactinoma.

#### REFERENCES

1. Check JH, Chase JS. Ovulation induction in hypergonadotropic amenorrhea with estrogen and human menopausal gonadotropin therapy. *Fertil Steril* 1984;42:919.
2. Check JH, Wu CH, Check ML. The effect of leuprolide acetate in aiding induction of ovulation in hypergonadism: a case report. *Fertil Steril* 1988;49:542.