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# **Pregnancy Following Sequential Bromocriptine Therapy in a Hyperprolactinemic Subject**

### Malachi J. McKenna, MD,\* M. Saeed-uz-Zafar, MD,<sup>†</sup> and Raymond C. Mellinger, MD<sup>†</sup>

Regular menses were maintained in a 26-year-old woman with a prolactinoma by sequential bromocriptine therapy given for either five or 14 days of the menstrual cycle. She conceived promptly when desired. (Henry Ford Hosp Med J 1987;35:192-3)

**D**rolactin-secreting pituitary neoplasms, a common cause of Pmenstrual irregularity and infertility, usually require therapeutic intervention. Except for some adenomas which may require surgery to reduce mass effect, administration of bromocriptine is generally considered the preferred method of management. Menses return and conception can be readily achieved in about 80% of treated subjects. However, medical treatment is not curative, and continuous administration is usually needed to maintain normal ovarian function. We report the successful use of sequential bromocriptine, administered prior to ovulation, in maintaining normal menstrual cycles and in making conception achievable in a patient with a prolactinoma.

### **Case Report**

A 26-year-old woman sought evaluation of oligomenorrhea and reduced libido which had been present for over two years. On examination, visual fields were intact to confrontation, and no hirsutism was present. Serum prolactin levels were consistently elevated between 298 and 379 ng/mL. She was euthyroid. Computed tomography of the sella turcica suggested a right-sided pituitary neoplasm. Bromocriptine was given, with the dosage gradually increasing to 2.5 mg twice daily. Her serum prolactin level fell to 22 ng/mL in one month. After two regular menstrual periods, the patient became pregnant, and bromocriptine was discontinued. Serial Goldmann fields remained normal during her pregnancy. A healthy baby was delivered at 38 weeks of gestation. Ten weeks postpartum, her serum prolactin level was 520 ng/dL, and bromocriptine was resumed at a dose of 2.5 mg twice daily for six months.

After six months of therapy, a trial of sequential bromocriptine administration was initiated to determine whether continuous control of hyperprolactinemia was necessary for preservation of cyclic ovarian function. The patient took 2.5 mg of bromocriptine twice daily from day 1 to day 14 of the menstrual cycle for 11 cycles and then took the same dose from day 1 to day 5 for two cycles. During the last cycle of therapy the patient discontinued contraception and consequent conception led to a full-term delivery of a second, healthy child.

Serum prolactin levels, measured by radioimmunoassay (Abbot Laboratories, North Chicago, IL), all were within the reference range (< 25 ng/mL) immediately following a course of therapy and all were elevated when tested during the weeks without treatment, ie, 110, 110, 140, and 160 ng/mL. Serum estradiol-17B, measured by radioimmunoassay of an extract (Radioassay Systems Laboratories, Carson, CA), and serum progesterone, measured by a commercial laboratory (Metric Medical Labs, Southfield, MI), were both evaluated in the luteal phase of four different cycles. Serum estradiol-17B levels were 130, 170, 210, and 260 pg/mL (reference range: 50 to 150 pg/mL), and respective serum progesterone levels were 9.0, 2.3, 10.9, and 15.4 ng/mL (reference range: 2.5 to 28.1 ng/mL).

#### Discussion

Over the past ten years, growing appreciation of the benign nature of microprolactinomas has led to conservative principles of management. In the past, transsphenoidal adenomectomy has often been recommended because of the fear of rapid tumor expansion, especially during pregnancy. The present trend is to provide symptomatic relief and to restore fertility by pharmacologic means. Restoration and maintenance of normal menstrual function indicate adequate estrogen production, which bromocriptine can provide. However, infertility, galactorrhea, and menstrual irregularity usually recur following discontinuation of bromocriptine.

Although it was demonstrated ten years ago that sequential bromocriptine therapy given during the follicular and periovulatory phase could induce ovulation and even result in pregnancy (1,2), such treatment is not routine. There is some

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evidence that the length of the menstrual cycle is prolonged if bromocriptine is not administered at the beginning of the cycle (2). However, the present case suggests that normalization of prolactin during the first five days can permit ovulation and thereby conception. One presumptive advantage of sequential therapy is that the fetus is not exposed to medication during the critical days immediately following conception. Although extensive experience has failed to show any teratogenetic effects, it is preferable to avoid drugs during pregnancy.

The mechanisms by which prolactin interferes with ovulation and menstrual functions are not entirely understood. However, disturbed ovarian function clearly results from abnormalities in the secretion of pituitary gonadotrophins. Our observation suggests that hyperprolactinemia may interfere with follicular recruitment rather than impair follicular maturation, ovulation, or corpus luteum function.

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