Gonadotropinoma presenting as a case of pseudo-ovarian failure changing to macroprolactinoma

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Summary

Purpose: To present the first gonadotropinoma presenting as pseudo-menopause in a teenager. *Methods:* Human menopausal gonadotropins (hMG) were given to a 37-year-old woman whose hypergonadotropic amenorrhea with estrogen deficiency as a teenager was changed to hypogonadotropic amenorrhea by the growth and prolactin secretion of a macroprolactinoma. *Results:* The patient responded multiple times, and every time to stimulation with hMG and each time produced several dominant follicles. She delivered two babies including conception at age 40. *Conclusions:* The fact that this woman could respond consistently to hMG 20 years after the diagnosis of premature menopause, it is clear that initially the etiology of the extremely high LH and FSH levels in an estrogen-deficient 18-year-old was the presence of gonadotropinoma secreting inert LH and FSH. Since serum prolactin was measured the first time at age 37, it is not clear whether the endogenous biologically active gonadotropine were suppressed by replacement of the gonadotroph cells with tumor cells or suppression of endogenous gonadotropins by hyperprolactinoma.

Key words: Gonadotropinoma; Hyperprolactinoma; Pituitary macroadenoma; Ovarian failure; Hypergonadotropic amenorrhea.

Introduction

The presence of a pituitary tumor causing supranormal circulating levels of one or both gonadotropins is not common [1, 2]. Less than 200 cases were reported by 1993 and not that many have been reported since that time [2].

These tumors are difficult to detect in postmenopausal women since gonadotropins are normally elevated in that group. Most of the time the gonadotropin hormones have normal physiologic function and in younger patients there have been 20 cases of gonadotropinomas causing ovarian hyperstimulation, and these cases have been summarized by the case report of Castelo-Branco *et al*. [3].

A case is presented which we believe is the first one ever described where replacement of normal gonadotrope cells by an follicle stimulating hormone (FSH) and luteinizing hormone (LH) secreting gonadotropinoma that secreted immunoreactive but biologically inactive gonadotropins led to the false diagnosis of premature ovarian failure.

Case Report

The patient had menarche at age 13 but had developed amenorrhea by age 18. She was estrogen-deficient as determined by failure to have menses with withdrawal of progesterone but a normal uterus and endometrium by having menses with oral estrogen followed by progesterone.

Evaluation found a serum FSH of 55 mIU/ml and LH of 42 mIU/ml. She was advised that having children with her own oocytes would not be possible, and she was continued on estrogen/progesterone replacement for ten years when she consulted a reproductive endocrinologist who confirmed the diagnosis of premature ovarian failure with a serum FSH of 78 mIU/ml and LH of 92 mIU/ml and placed her back on hormonal replacement.

At 35 years of age the woman consulted our group based on publications concerning methods of inducing ovulation in women with premature menopause [4]. Since the length of time from diagnosis to treatment correlates negatively with success in achieving ovulation in this group, the woman was advised about the poor prognosis [5]. However she still wanted to try the technique.

Off hormonal replacement her repeat gonadotropin levels were quite a surprise – her LH and FSH were < 1.0 mIU/ml and serum estradiol (E2) measured at 5 pg/ml. This prompted measuring serum prolactin which was markedly increased at 975 ng/ml.

Computerized axial tomography revealed a large pituitary mass with supracellular extension into both the sphenoid sinus and left middle fossa. At this stage the woman was considered inoperable and not a candidate for radiation therapy. She was then treated with bromocriptine and the tumor shrank to 50% of the previous size allowing transphenoidal hypophysectomy.

Though her prolactin level remained elevated even with 5 mg of bromocriptine per day being continued, there was no evidence of growth of the residual pituitary tumor.

The assumption was made that a woman with premature ovarian failure subsequently developed a macroprolactinoma which not only destroyed the gonadotrope cells but the high prolactin also contributed to bringing the elevated levels down to non-measurable levels. Nevertheless the woman wanted to try to conceive. The technique for reversing menopause involves lowering elevated FSH to restore FSH receptors in the paucity of the remaining follicles [6-8]. One possible explana-

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tion was that her initial diagnosis of premature ovarian failure was incorrect and all along she had a gonadotropinoma secreting biologically inactive gonadotropins which eventually became replaced by a macroprolactinoma. This concept was supported by the fact that she ovulated every cycle with human menopausal gonadotropins leading to several pregnancies with miscarriages but also two live deliveries. The last successful pregnancy was at age 40. She always produced multiple follicles.

Discussion

When women are able to reverse menopause they rarely ovulate every cycle and even when they do they usually make just one follicle. This patient ovulated every time with human menopausal gonadotropins and made multiple follicles. Considering the 20 year length of her amenorrhea it is clear that this was not a case of premature ovarian failure but rather a case of pseudo-premature ovarian failure related to the secretion of biologically inert gonadotropins that eventually converted to a macroprolactinoma.

We believe this is the first case where a gonadotropinoma was found that secreted biologically inert gonadotropins leading to a false diagnosis of menopause. Perhaps it is more common than this one case since if asymptomatic gonadotropinomas exist in postmenopausal women (i.e., no mass effects, e.g., headaches or visual disturbances) these tumors would go undetected. Since serum prolactin levels were never measured until age 37 when the FSH and LH were found to be low, it is possible that her own gonadotropin cells were not entirely replaced by the tumor cells but she did not secrete endogenous gonadotropins related to concomitant hyperprolactinemia. Many of the gonadotropinomas have been found to exist with hyperprolactinemia [3].

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