Pregnancy in a patient with premature ovarian failure

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Summary

Background: Premature ovarian failure (POF) occurs in about one in 100 women under 40 years of age. The authors report a case of a POF patient who conceived during hormonal replacement therapy (HRT). *Case:* A 24-year-old woman with confirmed POF conceived spontaneously during HRT.*Conclusion:* Pregnancy is possible in women with POF.

Key words: Premature ovarian failure, Hormonal replacement therapy; Pregnancy.

Introduction

Premature ovarian failure (POF) is defined as secondary amenorrhea, hypoestrogenism, and elevated levels of gonadotropins occurring in women before the age of 40 years [1]. The estimated incidence is one in 100 women under the age of 40, one in 1,000 women under the age of 30, and one in 10,000 women under the age of 20 [2, 3]. The etiology of most POF cases remains unknown (idiopathic POF). Known factors leading to this condition include X-chromosome anomalies, oocyte-specific gene mutations, autoimmune disorders, hypothyroidism, radiation, chemotherapy or surgery [4, 5]. Cessation of ovarian function in POF is not necessarily permanent. Young women with POF can experience intermittent and unpredictable resumption of ovarian activity and spontaneous pregnancies have been reported in about five to ten percent of cases subsequent to the diagnosis [6].

Case Report

A 21-year-old woman was referred to the present department because of secondary amenorrhea lasting for three years, irregular menses since the age of 16, acne, hot flashes, headaches, and moodiness. She had menarche at the age of 13 and reported regular menses, lasting four to five days, until the age of 16. After that her menses became irregular, the average cycle length was between 14 days and three months. She was treated with oral contraceptives since the age of 18. She had no history of chronic diseases and previous operations. The results of hormonal tests performed six months previously were: follicle stimulating hormone (FSH) 80.7 IU/l; luteinizing hormone (LH) 25.3 IU/l; etradiol (E2) 10.5 pg/ml. Her physical examination demonstrated a seemingly healthy woman with body mass index (BMI) of 23, Tanner stage V, small uterus during pelvic exam, including a hypoestrogenized vaginal epithelium. Transvaginal ultrasound revealed small uterus (2.9 cm length) with thin endometrium (four mm) and small ovaries (right ovary 4.9cm^3, left ovary 2.9cm^3) with a few follicles in the right ovary. Hormonal tests revealed FSH 90.9 IU/l; LH 35.9 IU/l; E2 8.5 pg/ml. Serum prolactin, thyroid and adrenal function tests were within the normal ranges. Karyotype was 46 XX. POF was diagnosed after clinical and ultrasonographic examinations and hormonal replacement therapy (HRT) with sequential two mg 17β-estradiol and ten mg dydrogesterone was proposed. HRT was continued for six years until secondary amenorrhea occurred during therapy. Ultrasonography performed two weeks later revealed the presence of gestational sac inside the uterine cavity with visualization of the embryonal tissue. Hormonal supplementation (ten mg dydrogesterone orally, twice a day) was administered for the next three months. Down syndrome and Trisomy 18 screening using biochemical and ultrasound markers performed at 13 gestational weeks were below the risk cut-off for these diseases. Pregnancy was uneventful aside from cholestasis of pregnancy, which was an indication for labor induction at 37 weeks of gestation. The patient delivered a healthy boy and her puerperium was uneventful.

Discussion

The possibility of spontaneous pregnancy in women with POF has been reported in about five to ten percent of cases [6], especially in case of fluctuating FSH levels, the possibility to identify ovaries on ultrasound, autoimmune POF or caused by chemotherapy [7]. Primary amenorrhea seems to be the worst predictive factor of intermittent ovarian function [8].

More than one-third of women with normal karyotype and idiopathic POF demonstrate appearances of ovarian follicles on pelvic ultrasound. Around 20% of these patients ovulate spontaneously during four months of observation, and nearly 50% of those affected have intermittent ovarian follicle function [9]. Pregnancy may occur after the diagnosis of POF, even in women with no follicles observed on ovarian biopsy [10].

The mechanism of possible pregnancy might involve the possibility of elevated gonadotropin causing downregulation of gonadotropin receptors and restoration of the sensitivity of the few remaining ovarian follicles by lowering of serum gonadotropin levels with estrogen therapy. Estrogen may increase the number and sensitivity of FSH receptors in granulosa cells and start the recruitment of follicles. Besides, gene coding for the FSH receptor or its regulatory enzymes may be augmented through activation of the hormone-sensitive adenylate cyclase and consequent elevation

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of the intracellular cAMP [11], what might explain the pregnancy in the presented presented case.

It is recommended that patients with POF are treated with HRT and are closely monitored for ovulation before resorting to oocyte donation. The combination of corticosteroids with pituitary suppression, followed by ovarian stimulation with gonadotropin, was shown to be beneficial in restoring ovarian function in patients with idiopathic POF. In patients with POF due to autoimmune disease, immunosuppressive treatments such as corticosteroids could improve ovarian function [8, 12]. Furthermore, bone marrow transplantation (BMT) was demonstrated to improve fertility in a portion of patients and in mice, but the mechanism by which BMT improves fertility remains unknown [13].

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