

Spontaneous pregnancy in a patient with a combination of ovarian and thyroid failure

Gravidez espontânea em uma paciente apresentando uma combinação de falência ovariana e disfunção tireoidiana

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SUMMARY

Premature ovarian failure has an overall prevalence of 0.3% to 0.9% in general population. If fertility is a concern, treatment usually consists of estrogen therapy as hormone replacement and oocyte donation. Spontaneous pregnancy in affected women is uncommon. We report a case of a 34-year old woman, who had premature ovarian failure and primary hypothyroidism, and conceived spontaneously eleven years after the development of premature ovarian failure and correction of hypothyroidism. *Arq Bras Endocrinol Metab.* 2011;55(4):291-3

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SUMÁRIO

A falência ovariana prematura tem uma prevalência global variando de 0,3% a 0,9% na população em geral. Nos casos em que existe preocupação com a fertilidade, o tratamento geralmente consiste de terapia de reposição hormonal com estrogênio e doação de óocitos. A gravidez espontânea em mulheres afetadas não é comum. Relatamos um caso de uma mulher de 34 anos de idade que apresentou falência ovariana prematura e hipotireoidismo primário e concebeu espontaneamente onze anos após o desenvolvimento da falência ovariana prematura e da correção do hipotireoidismo. *Arq Bras Endocrinol Metab.* 2011;55(4):291-3

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INTRODUCTION

The age of natural menopause is closely inherited and also affected by environmental factors. In average, menopause occurs at 51 years of age, with one percent of women continuing to menstruate beyond the age of 60 years. Premature ovarian failure (POF), or premature ovarian insufficiency, is usually defined as the cessation of menstrual cycles before the age of 40 years.

Diagnosis is based on elevated levels of follicle stimulating hormone (FSH) in menopausal range (usually above 40 IU/L), detected on at least two occasions a few weeks apart (1). Although normal menopause is an irreversible condition, approximately 50% of women with POF experience intermittent ovarian function and menstrual bleeding, after a period of secondary amenorrhea. Some women produce estrogen intermittently and ovulate, despite menopausal hormone levels (2). Pregnancy in women with hypergonadotropism and estrogen deficiency is less common. Though some cases

apparently occurred without any therapy, most of them involved women who had received some form of estrogen replacement (3-5). We report a case of a woman who conceived spontaneously 10 years after documentation of ovarian failure and subsequent correction of primary hypothyroidism.

CASE REPORT

A 34-year woman delivered her first child by cesarean section 14 years back, within the first year of her marriage. An intrauterine contraceptive device implanted at six months postpartum was removed after a period of two years. The subject failed to conceive and subsequently developed oligomenorrhea with hot flushes, followed by cessation of menstruation.

A diagnosis of premature menopause was made on the basis of postmenopausal levels of gonadotropins carried out four months apart (FSH was 36.73 IU/L and

41.93 IU/L). The patient was put on a cyclic combination of estrogen-progesterone (EP) (ethinylestradiol 0.03 mg and levonorgestrel 0.15 mg), which she continued for six years. Six years after the initial diagnosis of POF, measurement of gonadotrophins was repeated and was consistent with POF (FSH was 51.48 U/L). Besides, primary hypothyroidism (non-goitrous) was also detected, with serum thyroid stimulating hormone (TSH) of 25.48 μ U/mL (normal value 0.5-5) and thyroxine (T4) of 6.34 μ g/dL (normal value 5.5-13.5). The patient was further evaluated for any evidence of polyglandular failure or other autoimmune disorders. Complete blood count (CBC), erythrocyte sedimentation rate and blood chemistry, including liver and kidney function tests, were normal. There was no evidence of *diabetes mellitus*, adrenal or parathyroid hypofunction; testing for antinuclear antibody and rheumatoid factor was negative.

Patient continued on cyclical EP, and thyroxine 50 μ g P.O. was added. She continued these medications for the following four years until January, 2009, when EP treatment was discontinued because of weight gain and skin pigmentation. After stopping EP, she had three spontaneous menstrual cycles, followed again by amenorrhea. On a routine check-up, pregnancy was detected and confirmed by ultrasound examination, with gestational age of 9 weeks. The patient saw an obstetrician for her prenatal care.

She was again seen at the gestational age of 7 months, and investigations revealed hemoglobin of 11 gm/dL, serum calcium of 9.35 mg/dL (normal value of 9-11) and normal glucose tolerance. Her serum TSH was 2.7 μ U/mL (normal value 0.5-5), and free T4 was 1.11 ng/dL (normal value 0.7-2). Patient continued on 50 μ g of thyroxine. At gestational age of 38 weeks, she delivered a normal male baby of 3.2 kg and Apgar score of 8/10.

DISCUSSION

While normal menopause is generally an irreversible event, POF is characterized by intermittent ovarian function with estrogen production and even ovulation, despite the presence of high gonadotrophin levels. Chance of spontaneous conception ranges from 10 to 15% (3-5). Various therapies have been used in an attempt to induce fertility, including gonadotrophin releasing hormone agonists, sex steroids and corticosteroids. These interventions have failed to demonstrate any

significant improvement in ovulation and pregnancy rates (6). In general, the most appropriate recommendation for these individuals would be to consider donor oocyte with in vitro fertilization.

There are several isolated cases of spontaneous pregnancy in women with POF treated with estrogen (4,5,7-10). Alper and cols. reported six women who conceived after POF diagnosis. Two pregnancies occurred while on patients were on conjugated estrogen; two occurred while patients were on combined oral contraceptive pills, and two conceived spontaneously (3). There may be differences in fertility outcomes in women with ovarian failure, depending on the age of onset. In a retrospective analysis of 86 women with ovarian failure, 11% ovulated; and three conceived and delivered normal, healthy babies (11).

Spontaneous return of ovarian function can occur in women with an established diagnosis of POF, and no particular feature is able to predict this rare event with great accuracy. The case described here represents one of the longest intervals reported between the onset of POF and spontaneous conception. Despite hypergonadotropic hypogonadism, estrogen treatment may increase the likelihood of ovulation. There are several explanations for the usefulness of hormone replacement in these patients.

It was hypothesized that exogenous estrogen could act by lowering serum FSH and restoring the sensitivity of the remaining follicles, or by directly increasing the sensitivity of granulosa cells to the effect of FSH. Both actions would result in ovulation (12). Hormone therapy makes the uterus suitable for the implantation of the fertilized egg and subsequent pregnancy.

There are some anecdotal published reports that support the importance of actually lowering serum FSH. Despite high percentage of POF patients being treated with estrogen replacement, there is a paucity of published reports on pregnancies in these patients; higher doses of estrogen appear to work better (13). It has been seen that ovulation and conception are more common in women with one or two FSH measurements below 40 IU/L, as it was the case of our patient, in whom one FSH measurement at one of the three times was below 40 IU/L (FSH – 41.93; 36.73 & 51.48 IU/L).

A concurrent autoimmune disorder is present in 10%-30% of women with POF; with hypothyroidism as the most common one. Recovery of ovarian function may occur after regression of autoimmune state and

control of coexisting endocrine disease (6). The patient described here was also diagnosed with hypothyroidism and was treated with thyroxine, which also may have helped in ovulation and conception.

In summary, women with POF can conceive spontaneously long after confirmation of the diagnosis. Simultaneous correction of other endocrine deficiencies, especially thyroid failure, can help spontaneous conception.

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