Spontaneous Twin Pregnancy in Premature Ovarian Failure

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SUMMARY

Premature Ovarian Failure (POF) is associated with subfertility. Despite efforts to induce ovulation, success rates are low. We report a case of POF spontaneously conceiving twins while on hormone replacement therapy.

KEY WORDS:
Premature ovarian failure, Twin pregnancy, Hormone replacement therapy

INTRODUCTION

Premature Ovarian Failure (POF) is defined as menopause before the age of 40. It occurs with an incidence of 0.1% by the age of 30 and 1% by the age of 40[1]. Women with POF present with oligomenorrhoea or amenorrhoea. In women in their late thirties, the concern is the long term effects of menopause, mainly osteoporosis. Fertility is not usually an issue as these women. However, when POF presents in the twenties, fertility is the main concern as these women usually do not have any children yet and are only about to embark on marriage.

CASE REPORT

A 27 year old woman presented to a district hospital with amenorrhoea for 12 months. She attained menarche at the age of 13 and subsequently never had regular periods. Her periods were light and lasted for only 3 days, and her cycles were every 3-9 months. She was of normal build but had scanty axillary and pubic hair. Her breasts were of Tanner stage 4. Pelvic examination was normal. A pelvic ultrasound showed a normal sized uterus but the ovaries were not definitively seen. Her serum tests were: FSH 86.2 mIU/ml, LH 33.1 mIU/ml and prolactin 106.3mIU/ml. These levels were repeated 3 months later with similar findings. Her karyotype was 46XX. Other investigations that were also normal were serum DHEA, testosterone, anti-nuclear antibodies and an intravenous urogram. A diagnosis of premature ovarian failure was made. She was told that she was unlikely to ever become pregnant and was started on hormone replacement therapy (estradiol valerate 2mg and norgestrel 500mcg) to prevent the long term sequelae of POF.

She married the following year and was keen to have children. A diagnostic laparoscopy and dye insufflation test was performed which revealed a small uterus and small streaky ovaries. Both fallopian tubes were patent. No ovarian biopsy was taken as the appearance of the ovaries was consistent with premature ovarian failure. She continued with her previous regime of HRT.

Later in the year her HRT was changed to conjugated oestrogen 0.625 mcg and medroxyprogesterone acetate 5 mg cyclically. Six months on this new regime, she presented with amenorrhoea and she was found to be six weeks pregnant with dichorionic diamniotic twins. She was put on dydrogesterone 10 mg twice daily till 16 weeks gestation to support the pregnancy until placental function was established. The pregnancy progressed uneventfully until she went into labour at 36 weeks gestation. A caesarean section was performed and she delivered a healthy baby boy and girl. The babies weighed 2.3 kg and 2.25 kg respectively. She managed to breastfeed her babies up to two months, when she stopped as she went back to work.

Following delivery, she was amenorrhoiec for 16 months when she came again for follow up. Her serum profiles were similar to the levels when she was first diagnosed with POF, and her serum oestradiol was 44.0 pmol/L. Her thyroid function was normal. As she was not planning further pregnancies at present, she was put on the oral contraceptive pill.

DISCUSSION

The pathophysiology of POF is believed to differ from the normal menopause process. In the latter, ovarian function gradually declines and this change is permanent. Women with POF on the other hand, tend to experience intermittent ovarian function, and remissions and pregnancies are possible. In ovarian failure (premature or menopause), the ovaries produce only small amounts of oestrogen or none at all (serum oestrogen <25 pg/mL). This results in loss of negative feedback to the hypothalamus and pituitary glands. The pituitary gland therefore produces elevated levels of FSH (>40 mIU/ml)

There are case reports of pregnancies in affected women. Spontaneous conceptions are estimated to be only 5-10%[2]. Most reports have been in women while on HRT or after stopping the oral contraceptive pill (OCP). The suggested mechanism is that oestrogen may increase the number and sensitivity of FSH receptors in the granulosa cells and start the recruitment of follicles. This is opposite to what happens in POF where high FSH levels cause down-regulation of the FSH receptors.

In our case report, what is interesting is that this woman not only conceived on HRT, but by conceiving dichorionic diamniotic twins, she had produced at least two ovarian follicles.

This article was accepted: 20 May 2008
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Literature on ovulation induction in POF is limited to small studies. None are linked to HRT. The majority of studies are done using different regimes of ethinyl oestradiol and even then, results are contradicting. Buckler *et al*[3] showed there was no benefit of the oral contaceptive pill in subsequently inducing ovulation. Check *et al*[4] reported a 60% ovulation rate in women treated with ethinyl oestradiol alone without ovulation induction, but pregnancy rates were unchanged. However, a randomised controlled trial by Tartagni *et al*[5] showed a 32% ovulation rate and 50% pregnancy rate ($p<0.0050$) when women were pre-treated with ethinyl oestradiol and then ovulation was induced with recombinant FSH.

In conclusion, women with POF can achieve successful pregnancies by down-regulation of FSH using HRT. This is important not only as a fertility treatment but also emphasizes the importance of putting women with POF who are not planning pregnancies on OCP rather than HRT.

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