J Obstet Gynecol Ind Vol. 53, No. 3 : May/June 2003 Pg 290-291

A Spontaneous Successful Second Pregnancy in an Established Case of Premature Ovarian Failure.

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Key words : premature ovarian failure.

Introduction

Reported here is the case of a woman with premature ovarian failure (POF), who had her first child through HRT and donor oocyte programme and who spontaneously conceived and subsequently delivered her second child.

Case report

A 22 year old woman was referred to us with secondary amenorrhoea and infertility. She attained menarche at the age of 13. Since then she was menstruating regularly for five years after which her cycles became gradually irregular and she was advised progesterone for withdrawal bleeding. She responded well initially and then stopped responding to progesterone after which she had to be administered cyclical estrogen and progesterone to regularize her menstruation. On examination, she was found to have normal growth and secondary sexual characteristics, with normal karyotype. Her basal hormone levels recorded at our centre were LH 13.22 mIU /ml, FSH = 34.21 mIU/ml, Prolactin = 9.14 Ng/ml, T3 1.02 ng/ml, T4 = 5.7 µg/dl, TSH 2.18 µIU /mL and free T4 = 1.13 ng/dl. Diagnostic laparoscopy showed streak ovaries with hypoplastic uterus and normal fallopian tubes which confirmed that she was a case of premature ovarian failure (POF). She was advised HRT and donor oocyte programme. Her husband's semen analysis showed count of 60 million with 40% active motility. We started her on cyclical conjugated estrogen and allylestrenol therapy to attain minimal uterine size of 6.0 x 3.0 cms which seems to be optimal for conception. She was then taken up for a donor oocyte program. Pregnancy was achieved in the fourth attempt by ET, the previous two attempts of ET and one GIFT procedure having been unsuccessful. Pregnancy was uneventful and she delivered a live female baby by elective cesarean section in April 2000.

Paper received on 28.12.02 ; accepted on 31.7.02

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She returned with six months amenorrhoea following delivery, wanting to regularize her cycles. She was put on a similar cyclical steroid therapy (conjugated estrogen and allylestrenol). She had regular cycles for a period of six months after which she came back with a history of amenorrhoea for two months. Her hormonal analysis was normal and a pelvic ultrasound confirmed pregnancy with a single intrauterine gestational sac corresponding to her period of amenorrhoea. Her antenatal period was uneventful. She delivered her second female baby in August 2001 by elective cesarean section.

Discussion

POF is a condition causing amenorrhoea, hypoestrogenism, and elevated gonadotrophins in women younger than 40 years of age. Failure means absence of normal ovarian function, but not necessarily total cessation of ovarian function. Patients with premature ovarian failure may intermittently produce estrogen and even ovulate, albeit at abnormally high serum gonadotrophin levels. It may also be reversible.

There have been a few reported cases of secondary amenorrhoea and elevated gonadotrophins, who several months later, resumed normal menstrual cycles[1-4]. This has been associated with the use of estrogen therapy, suggesting that the estrogen may activate receptor formation on follicles and the high gonadotrophins may thus stimulate follicular growth and development. On the other hand, temporary recovery of ovarian function may be the reason for the apparent success with treatment. In some patients, a return of normal ovarian function with pregnancy has occurred spontaneously. While resumption of normal function is extremely rare, it is now necessary to counsel the patients who fit into this category that there is a very remote possibility of spontaneous pregnancy in future.

Patients with POF need cyclic estrogen and progesterone therapy to relieve symptoms of estrogen deficiency, to maintain bone density and to reduce the risk of cardiovascular diseases[5]. To date there is no intervention to induce ovulation in patients with POF, but nearly 20% of these patients will ovulate during a period of

four months of observation[4]. Recently, a study showed that pregnancy will occur subsequent to the diagnosis of POF in approximately 10% of the patients[2].

Molecular genetics and recombinant technologies are powerful advances to improve our understanding of POF. Ovarian biopsies are less frequently performed because of problems with sampling error. Pregnancies have occurred despite laparotomy specimens demonstrating no primordial follicles or even streak ovaries[1,2,5]. These women may now be able to achieve a pregnancy with donor oocyte programme. Excellent results of 27 pregnancies out of 100 donor oocyte cycles have been reported[6].

In 1982, Rebar et al[7] reported follicle function in 9 out of 18 women previously diagnosed with POF. Although most POF occurs sporadically, a family history of POF is found in 4% of patients [2,8,9]. Ten to fifteen percent of patients with POF present with primary amenorrhoea[2,4]. In patients with no chromosomal abnormality, the pre-pubertal growth and secondary sexual characteristics were found to be normal[10]. Some of the patients have had only a few, scanty menses at the time of menarche[11].

During a two-year period we had 180 cases of POF amongst 3600 infertile patients. One hundred cases came for regular follow up. Excluding six cases who did not have improvement in uterine size and blood flow, we achieved 30 pregnancies in 94 patients (31.9%). It is evident that it is worthwhile treating cases of POF with donor oocyte programme since the pregnancy rate is quite rewarding and there is always a possibility of spontaneous pregnancy following cyclical estrogen and progesterone for regularizing the menstrual cycle. The obstetric performance in the POF patients is always risky since their uterus had already shrunk to an infant size and had to be re-grown to a little more than 6 x 3cms. The uterus is very sensitive and therefore preterm delivery is more common when compared to the general population and the perimenopausal group. Six of our 30 patients (20%) delivered prematurely, four at 32 weeks and two at 36 weeks.

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