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Successful Pregnancy Outcome in Primary Amenorrhoea

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Abstract: ***Background: Women diagnosed with premature ovarian failure frequently receive hormonal replacement therapy as a vital part of the management protocol. nevertheless, it is very unusual for patients to get pregnant while on hormonal therapy. Case: A 20-year-old woman with a history of primary amenorrhea and under developed secondary sexual character was diagnosed with premature ovarian failure. Part of her amenorrhea workup included hormonal level estimation, karyotyping ,laparoscopy and bilateral ovarian biopsy. She was started on HRT when she attained menarche and developed secondary sexual characters. Two years later she got married and conceivied with the very first cycle of IVF, and a successful outcome of a twin gestation. Conclusion: The etiology of premature ovarian failure is unknown most of the time. In scarce cases this condition undergoes spontaneous, reversible remission. Most of the women with POF can achieve successful pregnancies with HRT but on the failure of HRT a successful pregnancy can be acheived with IVF is what was observed in our case.***

Keywords: primary amenorrhoea; premature ovarian failure; HRT

1. Introduction

Amenorrhea is the absence or abnormal cessation of the menses [(1)]. Primary and secondary amenorrhea describes the occurrence of amenorrhea before and after menarche, respectively. Most causes of primary and secondary amenorrhea are similar. Need of evaluation of primary amenorrhea is indicated when there has been a failure to menstruate by age 15 in the presence of normal secondary sexual development (two standard deviations above the mean of 13 years), or before five years after breast development if that occurs before age 10 [(2)].

Average age of the menopause is 50 years [(3)] with 1% of women menstruating even after the age of 60 years and 1% entering menopause before the age of 40. Environmental and hereditaryfactors affect the age of the menopause. A menopause before the age of 40 is commonly defined as "premature ovarian failure" although this definition is arbitrary. Estimates of the prevalence of premature ovarian failure range between 0.3 and 1% and this also accounts for 10–28% of women with primary amenorrhoea and 4–18% of women with secondary amenorrhoea [(4)].

10 to 30% of women with POF ia associated with a concurrent autoimmune disorder,out of which the most common is hypothyroidism. Thus, a complete history to exclude symptoms of other autoimmune disorder like Addison's disease, hypothyroidism and diabetes should be done. In the future these women who are diagnosed as POF should be monitored for the later appearance of these conditions.

History which are helpful in determining aetiology of ovarian failure such as positive family history, a concurrent autoimmune disorder, stress, or stigmata of one of the inherited conditions. In many instances a formal pedigree enquiry is required to determine other female family members who may be affected, particularly if the inheritance is passed through an unaffected male.

Netter et al have suggested that sever emotional stress could be cause of POF [(5)]. Even though there is a absence of controlled evidence for a specific population, physiologic replacement of ovarian steroid hormones seems rational until the age of normal menopause [(6,7)]. Temporary return of ovarian function, as indicated by elevated estrdiol levels, follicle development, and even pregnancy may occur in women with idiopathic, iatrogenic ovarian failure [(5-9)]. Here, we report a case of POF who attained menarche and developed secondary sexual characters following hormone replacement therapy, and concieved by IVF.

2. Case Report

A 20 year old woman presented to the obstetrics and gynecology opd with primary amenorrhoea, she was never investigated till this age due to the guilt of being blamed. Physical examination: height 160 cm, weight 58 Kg , BMI 22.65 Kg/m^2, cranic, and upper and lower limb measurements between 50° and 75° percentile. No alterations detected in fingers and toes.She was of normal built but had scanty axillary and pubic hair. Her breasts were of Tanner stage 2. Facial features revealed no dysmorphisms, moreover neither mental impairment or cognitive deficit was evident. Vital signs were normal.

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A pelvic ultrasound showed a infantile uterus with steak ovaries. Her serum tests were: FSH 65 mIU/ml, LH 30 mIU/ml and prolactin 101mIU/ml. These levels were repeated 1 months later and found to have similar findings. Her karyotype was 46XX. Few other investigations that were also normal were serum DHEA, testosterone, anti-nuclear antibodies and an intravenous urogram. A diagnosis as premature ovarian failure was done after a laproscopic biopsy of the ovary showed the presence of the follicles . She was treated with cyclical hormonal therapy and attained menarche after 3 months of the initiation of the therapy . She married after 2 year and was keen to have children. 12 months later patient wanted to conceive and insisted on IVF due to family pressure. With the very first cycle of the IVF patient conceived a DCDA twin gestation.5 . 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 as patient presentated with PPROM and first twin ws found to be breech and second was cephalic. Patient delivered a healthy baby boy of 2.2kgs and girl of 2.3 kgs. Following delivery, she was amenorrhoiec for 24 months and when she came again for follow up. Her serum profiles were similar to the levels when she was first diagnosed with POF. The patient had no intension of further pregnancies she was put on the oral contraceptive pill.

3. 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 atall (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). Women with POF are not always sterile;they still have 5% chance of conceiving at some timeafter diagnosis [6].The terms "hypergonadotropichypogonadism" and "premature ovarianinsufficiency" are more accurate, than premature ovarian failure.Majority of the spontaneous pregnancies occur whilepatients are receiving HRT, but this may not implya cause-and- effect relation [7].

Our patient had never been investigated till the age of 20 years for primary amenorrhoea and under developed secondary sexual charecters. As most of the other blood investigations where with in normal limits the exact cause of the premature ovarian failure was not detected. Although, we know that ovarian "failure" in POF does not mean permanent cessation of ovarian function, but the likelihood of recovery of ovulation is not possible to predict POF [7]. Although, different drug intervention such as various dosage of corticosteroids, estrogen, clomiphene, high-dose gonadotropin, recombinant FSH, danazol, and apoptatic inhibitors were recommended to induce ovulation in patients with POF, " but the few randomized controlled trials that are available fail to demonstrate any significant improvement in ovulation and pregnancy rates[7,9]. Assisted conception (IVF) with donated oocyte was documented to be choice inthese patients [6,7]. Advanced in technology of cryopreserved ovarian tissue transplantation and in-vitro maturation of oocytes derived from stem cells, may make it possible for some women with POF to use their own egg for IVF [10,11]. The women with a significant family history of POF may consider oocyte or embryo cryopreservation since there are currently no entirely reliable tests to predict ovarian reserve [12,13]. Pregnancy in the patients with POF is associated with significant fetal and maternal mortality and morbidity such as increased risk of a child with fragile X syndrome, intra uterine fetal death, pregnancy-induced hypertension, and postpartum adrenal crisis [14 - 16]. So women who wish to avoid pregnancy should use a barrier method, because HRT or use of oral contraceptive pills will not prevent conception, perhaps due to the elevated gonadotropin levels in this condition [17].

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