Spontaneous Pregnancy and Live Birth by a Patient with Premature Ovarian Failure: A Case Report

Rawan Abdulrahim Abduljalil, MB BCh BAO, MRCOG* Ammar Chiter, PHD, Msc** Huda Sharida, MBBS, FRCOG*** Nawal Dayoub, MD, FRCOG, MSc****

ABSTRACT

Premature Ovarian Failure (POF) or premature ovarian insufficiency (POI) is the loss of ovarian function before the age of 40. It is a very stressful condition as it has a critical impact on a patient's fertility potential. Around 5-10% of women with POI may have a spontaneous pregnancy, but many may require multiple attempts at in vitro fertilization (IVF) to achieve a successful pregnancy. Nevertheless, the only effective treatment approach to achieve pregnancy resides in oocyte donation for these women. We present a case of spontaneous pregnancy in a woman diagnosed with premature ovarian failure. The outcome of the pregnancy was a healthy term baby delivered vaginally.

Keywords: Early menopause, Infertility, Live birth, Premature ovarian failure, Spontaneous pregnancy.

INTRODUCTION

Premature Ovarian Insufficiency (POI)—also known as Premature Ovarian Failure (POF)—is the loss of ovarian function before the age of 40[1]. It is a very stressful condition as it has a critical impact on a patient's fertility potential. Follicle Stimulating Hormone (FSH) is an important hormone for the reproductive system that is released by the pituitary gland and is responsible for ovarian follicle growth[2]. The presence of non-responding follicles due to POF leads to increased levels of FSH. Anti-Müllerian Hormone (AMH) is produced by the granulosa cells in the follicles and reflects the number of follicles available, with a higher level meaning a greater number of follicles present[1].

According to the European Society of Human Reproduction and Embryology (ESHRE), POI is characterized by the presence of amenorrhea for at least four months, low oestrogen, and high gonadotropin levels (FSH > 25 mIU/ml) before the age of menopause[1,3]. The prevalence of POI varies according to age. It occurs in approximately 1 in 10,000 women younger than 20 years (0.01%) and affects 1 in 100 women by the age of 40 (1%)[1,4,5]. At the age of 20 weeks of gestation, the female foetal ovaries contain around 6 to 7 million oocytes, but this number falls gradually until birth, when only 300,000 to 400,000 oocytes remain[6].

POI is mostly caused by normal aging but can be due to genetic conditions, such as Turner syndrome, fragile X syndrome, and translocation of the X chromosome[1,7,8]. It can also be caused by iatrogenic factors (ovarian surgeries, radiotherapy, and chemotherapy)[1,9], autoimmune hypothyroidism, rheumatoid arthritis, Sjögren's syndrome, adrenal insufficiency, myasthenia gravis, systematic lupus erythematosus[1,10] metabolic factors (galactosemia and 17-hydroxylase deficiency)[10], infectious factors (human immunodeficiency virus, mumps, cytomegalovirus, and pelvic inflammatory diseases)[1,11], or environmental factors (pollutants and toxins)[12]. Around 5 -10% of women with POI may have a spontaneous pregnancy. However, many may require multiple IVF attempts to achieve a successful pregnancy[1,3,13]. The only effective treatment approach to achieve pregnancy resides in oocyte donation for these women.

CASE PRESENTATION

A 29-year-old Bahraini female was referred from a local health centre for full investigations and assessment. She had a 3-year history of secondary amenorrhea and high FSH levels. Menarche occurred at the age of 15 years with regular periods up until 3 years prior. She had no notable medical, surgical, or family history and no known cases of any allergies. Her husband was 31 years old, he was a non-smoker, and he had no notable medical, surgical, or family history.

Laboratory investigations showed elevated FSH levels at 86.6 mlU/ml. Her Luteinising Hormone (LH) levels were 63.2 mlU/ml with very low AMH at < 0.16 mlU/ml. Thyroid Stimulating Hormone (TSH), androgen, prolactin, immune testing results, and karyotype were all normal. Ultrasound examination of the pelvis showed no pathology. The results obtained confirmed a diagnosis of POF.

Full counselling was provided following the diagnosis, and the patient was advised to start hormonal replacement therapy (HRT). Oocyte donation is culturally and religiously not an acceptable practice in Bahrain. Adoption was also not considered by the couple at the initial counselling. The patient was advised to continue with her attempts at

* Resident
Department of Obstetrics and Gynecology
BDF Hospital, Bahrain
E -mail: rae10452@rcsi-mub.com
** Senior Embryologist
Banoon ART and Cytogenetics Centre
BDF Hospital
Bahrain
*** Consultant Obstetrician and Gynaecologist
Head of Department, Alsalam Hospital
Bahrain
**** Consultant Obstetrician and Gynaecologist/ IVF
London

natural conception as spontaneous recovery of ovarian function could still happen, given her young age.

The patient was followed up in the outpatient clinic almost every 6 months to recheck her FSH levels. The range of her FSH levels varied between 29 and 78 mlU/ml. She had an unexpected spontaneous pregnancy after 4 years of infertility with amenorrhea. Her last withdrawal period before pregnancy involved only 3 days of light bleeding. During her first trimester, she experienced per vaginal spotting, which was managed with supportive progesterone (Duphaston Abbott 10-mg oral tablets twice daily).

Her pregnancy was uneventful with a normal anomaly scan at 22 weeks. At 36 weeks of gestation, she was admitted for induction of labour due to reduced foetal movements. For prophylaxis against neonatal acute respiratory distress syndrome (ARDS), she received dexamethasone sodium phosphate (2 doses of EIPICO 12 mg every 12 hours). She was induced with prostaglandin E2 (Pfizer Prostin 3-mg vaginal suppository). She had a normal spontaneous vaginal delivery of a live and healthy baby girl weighing 2.900 kg. Her FSH level was high post-delivery, reaching 28-40 mlU/ml.

DISCUSSION

The incidence of chromosomal abnormality in patients with POI is approximately 1 in 2000 to 1 in 2500 females[14] Rafique et al. reported a 31-year-old nulliparous woman with primary infertility for 5 years. She was investigated and found to have premature ovarian failure with trisomy X syndrome (47,XXX)[15] Yuan et al. presented three adolescent patients aged 14, 15, and 14 years who were diagnosed with premature ovarian failure. They were found to have new microdeletions in chromosomes 15q25.2, 19p13.3, and 16P11.2, respectively, which was confirmed by chromosomal microarray analysis (CMA)[16].

Hashem et al. reported the first case of a reciprocal autosomal chromosomal translocation t(5;13) in a 39-year-old primary infertility patient diagnosed with POI, which was the 10th case of reciprocal translocation[17]. Wanyoike-Gichuhi et al. reported 29-year-old twin patients who were both diagnosed with POI. Chromosomal analysis was not done for the twins to analyse the cause of POI, but it was most likely genetic[18]. Unfortunately, once chromosomal abnormality has been detected, the patient is unlikely to conceive.

Endometriosis can lead to a reduction in pregnancy potential through a wide range of means. The most detrimental mechanism is the presence of ovarian endometrioma. A systematic review and meta-analysis of the effect of ovarian endometrioma on ovarian reserve found that the presence of endomterioma negatively impacts the ovarian reserve. However, the same review found that endometrioma has no effect on pregnancy and live birth rates[19,20].

The impact of ovarian surgery can be detrimental on the number of remaining follicles. Guler et al. compared operated and intact endometrioma. They reported that cancellation cycle rates were higher in the operated group, which had lower pregnancy rates and numbers of embryo transfers. They found no statistical significance among live birth rates per cycle and per ET, and they concluded that laparoscopic operation may worsen reproductive assistance technology by decreasing ovarian reserve[21,22]. On the other hand, Opøien et al. concluded that laparoscopic surgical removal of endometriosis improves assisted pregnancy outcomes in mild to moderate cases[23]. Other studies found no benefit of endometrioma resection for IVF success rates[24-26].

The inability to conceive is a major concern in women diagnosed with POI, particularly in very young patients. Many patients request IVF treatment with the hope of improving their chances of conceiving. FSH levels and the antral follicle count (AFC) are key indicators of ovarian reserve. Some studies suggest that high FSH levels lead to impaired quality and quantity of follicles, which are ready to be stimulated. They are also suggested to affect the number of oocytes retrieved and implantation rate following IVF or intracytoplasmic sperm injection (ICSI) procedures[27-29]. However, other studies have failed to find such a relationship[30,31].

A study carried out by Özelçi et al. explained the clinical characteristics of IVF cycles in women with poor ovarian reserve (POR). They examined 3 groups: one with diminished ovarian reserve due to a previous ovarian surgery, one with early ovarian aging, and one with age-related diminished ovarian reserve. They concluded that there were no statistically significant differences between the 3 groups regarding cancellation cycle rate, clinical pregnancy rate, implantation rate, mature oocytes, and many other factors. It is worth noting that those with younger age and lower FSH levels had higher pregnancy rates[29]. Spontaneous pregnancy occurs in approximately 5-10% of women diagnosed with POI. Calik-Ksepka et al. reported a 27-year-old woman diagnosed with POI who was on HRT. After 6 months, she conceived spontaneously[32]. Similar cases were reported of a 27-year-old woman receiving HRT who spontaneously conceived diamniotic twins, as well as a 30-year-old woman who conceived spontaneously after 4 years of HRT therapy[33,34].

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