

Polycystic Ovarian Syndrome and Subsequent Diminished Ovarian Reserve: A Case Report

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Abstract

Background: Both PCOS and DOR are common diseases of abnormal ovarian reserve function in reproductive centers. In recent years, the incidence of PCOS and DOR has been on the rise, seriously affects women's reproductive health and quality of life.

Case presentation: A 35-year-old woman who was originally a PCOS patient became a PCOS combined with DOR patient in the following years after she successfully gave birth to a child through ovulation induction. She wanted to have a second child, so she came to our reproductive center for help again. She did not pregnant after 3 months of ovulation induction in our reproductive center outpatient clinic until she received IVF-ET treatment in the reproductive center.

Conclusions: Pregnancy counseling and infertility treatment should be considered early for women with PCOS, so as to avoid delaying the best time of pregnancy. If PCOS further develops into DOR, it will increase the difficulty of pregnancy, and also make patients spend more time and energy to achieve a successful pregnancy.

Keywords: Diminished ovarian reserve (DOR); Polycystic ovarian syndrome (PCOS)

Introduction

Polycystic ovary syndrome (PCOS) is one of the most common endocrine diseases affecting women of childbearing age, with a prevalence of about 5%-10% [1]. There are plenty of reports on the incidence of PCOS in different populations. The prevalence of PCOS in people of childbearing age in China is 5.61% [2]. It is reported that PCOS is the main cause of ovulatory dysfunction related infertility [3]. Diminished ovarian reserve (DOR) refers to the reduced ability of the ovaries to produce oocytes, resulting in a reduced number of oocytes, slow development, decreased quality, and reduced levels of sex hormones secreted by the ovaries, leading to a decrease in fertility in women. Its clinical manifestations are menstrual cycle disorder, low menstrual volume, abnormal uterine bleeding, infertility and so on.

Women with PCOS usually have higher luteinizing hormone (LH) and lower Follicle-Stimulating Hormone (FSH) levels in the early follicular phase compared to normal women⁴. Besides, serum Anti-mullerian hormone (AMH) levels are increased significantly in women with PCOS when compared with normal ovulation women [5,6]. However, we find a PCOS patient with higher FSH/LH ratio in our clinical work. Meanwhile, the level of her serum AMH level is lower. It seems to be a paradox. PCOS patients appear to present with DOR. Former studies have focused on the comparison of hormones between PCOS and DOR patients, but until now, to our knowledge, there are no published reports in international papers about PCOS patients with subsequent DOR. Therefore, the following case demonstrates a unique presentation of a patient of PCOS and with subsequent DOR.

Case presentation

A 35-year-old woman presented to our reproductive center due to secondary infertility. This patient was diagnosed with PCOS in 2013. She was treated with ovulation induction in the outpatient department of our hospital because of ovulation disorder. After 3 months of ovulation induction, she successfully became pregnant. She gave birth to a girl by cesarean section in 2014. After that, she had normal sex life with her husband and had not been pregnant for more than 3 years without contraception. The patient was 160cm in height, 70kg in weight, and 27.34kg/m² in BMI. The average menstrual cycle was 30-50 days, and the menstrual period was 7 days. The patient suffered from

hirsutism, obesity, amenorrhea, and impaired glucose tolerance (IGT).

She wanted a second child, so she came back to our reproductive center for help in 2020. At the time, her AMH level was 0.910ng/ml. The basic sex hormones on the second day of menstruation indicated: FSH:7.44mIU/ml, LH: 2.2mIU/ml, E₂:95pg/ml, progesterone(P): 0.42ng/ml. Sinus follicle count (AFC) of bilateral ovaries < 5, combined with her AMH, FSH and LH levels, she was diagnosed as DOR. No abnormalities were observed in hysterosalpingography (HSG). No abnormal thyroid hormone and related antibodies were found. Her husband's semen was analyzed in our hospital and found no abnormality. Chromosome examination of them in our hospital showed no abnormality. After 3 months of ovulation induction in the outpatient clinic, the patient failed to get pregnant and was treated with IVF-ET in the reproductive center.

According to the number of basal follicles, BMI, age, and previous ovulation induction, the basic sex hormone levels and the number of AFC in bilateral ovary (AFC < 5) on the second day of menstruation of the current cycle, the antagonist regimen was used for ovulation induction. Ovulation induction was started on the 2nd day of the menstrual period, and a total of gonadotropins (Gn)1650IU was used in this cycle. The levels of FSH, E₂ and P on trigger day were 8.09 mIU/ mL, 1536 pg/ mL and 0.55 ng/ mL, respectively. Nine oocytes (all mature oocytes) were aspirated from 11 follicles with 4000 u HCG and 0.2mg Triptorelin Acetate (Diphereline, IPSEN PHARMA BIOTECH) trigger.

We did regular in vitro fertilization (IVF). Nine oocytes were obtained and all were used in IVF. Eight embryos were obtained, while four embryos were usable. There were three good embryos. Two fresh embryos were transplanted. Two weeks later, β -HCG was 820.24mIU/ml, suggesting a successful pregnancy. Transvaginal B-ultrasound was performed four weeks later, suggesting that pregnancy sac with an inner diameter of about 21mm*25mm*9mm, germ with a length of about 3.5mm, original cardiac tube pulsation and yolk sac with a diameter of 4mm can be seen in the uterine cavity. The patient had an uneventful pregnancy and delivered a healthy, normal male infant weighing 3600g by elective cesarean section at 38 weeks of gestation.

Discussion and conclusions

In this case, we reported a patient who developed from a simple PCOS patient to a patient with PCOS combined with DOR, and succeeded in pregnancy after treatment with IVF-ET. In 2013, the AFC of this patient was around 14-16, while in 2020 her AFC was < 5, and the ratio of FSH/LH was significantly higher than that in 2013 (Basal hormone in 2013: FSH: 4.23 mIU/ml, LH 2.51 mIU/ml, E₂ 327 pg/ml, Basal hormone in 2020: FSH: 7.44 mIU/ml, LH: 2.2 mIU/ml, E₂ 295 pg/ml, P 0.42 ng/ml), and AMH was only 0.91 ng/ml. However, this patient still has significant clinical manifestations of PCOS, such as hirsute, irregular menstruation and ovulation disorder, so now she is a patient with PCOS combined with DOR. It is generally believed that PCOS patients belong to patients with high ovarian reserve, and generally do not have to worry about the absence of follicles. This patient is a warning to us that even patients with high ovarian reserve, such as PCOS, may become low ovary reserve.

Common clinical manifestations of PCOS include irregular menstruation, hyperandrogen-related manifestations, ovulatory dysfunction and infertility, etc., which may also be accompanied by metabolic abnormalities such as obesity, insulin resistance, hyperinsulinemia, glucose and lipid metabolism disorders. Our patient presented as follows: thin menstruation (thin ovulation), hirsute (clinical manifestation of high androgen), accompanied by obesity (BMI 27.34), abnormal glucose tolerance, and insulin resistance, according to Rotterdam diagnostic criteria [7], she was diagnosed as PCOS. At present, there is no unified diagnostic criteria for DOR in all parts of the world. In our clinical work, the diagnostic criteria for DOR are usually as follows: 1. FSH > 10 IU/L or FSH/LH > 3 or bE₂ > 80 pg/ml [8]. 2. Any risk factors for POR and/or abnormalities in ovarian reserve testing, such as AFC < 5-7, AMH < 0.5-1.1 ng/ml [9]. According to the AFC, FSH/LH, and AMH of this patient, the diagnosis of DOR was confirmed.

This case suggests that patients with PCOS are at risk of a decline in reserve function with age. It has been reported that Taiwanese women with a history of PCOS are more than 8 times more likely to develop DOR than women without PCOS. Although PCOS is a group with ovulation disorder, compared with the group with DOR, it is still relatively easy to get pregnant. The successful pregnancy rate can be obtained either in out-patient ovulation induction or IVF. However, for DOR population, because of less follicle development and poor follicle quality

compared with the same age, the probability of pregnancy is lower than the normal population. The pregnancy rate of DOR was also lower than that of PCOS. In general, younger patients with DOR have better follicle quality than older patients with DOR. Our PCOS patient developed DOR at the same time, and there is not much literature on PCOS combined with DOR at present. The purpose of publishing this case report is to hope that clinical reproductive doctors will pay more attention to the clinical diagnosis and treatment of PCOS combined with DOR.

The pathogenesis of PCOS is not fully understood, and may be related to hyperandrogenemia (HA), insulin resistance (IR), LH and FSH imbalance, metabolic abnormalities, inflammation, etc [10]. DOR mainly occurs in women over 40 years old under physiological conditions. The causes of DOR in women under 40 years old mainly include genetic factors, immune factors, enzyme deficiency, ovarian destruction factors, environmental factors, mental and psychological factors, etc [11-13]. According to the current research results, there is no clear pathogenesis of PCOS combined with DOR. Most scholars believe that the disease is mainly related to genetic factors, endocrine and metabolic disorders, environmental factors, mental and psychological factors, etc. In our case, the patient had no immune abnormalities and no bad habits such as smoking, while the patient's mother had early menopause and had a genetic tendency to ovarian dysfunction. Besides, she was associated with obesity, insulin resistance and other endocrine and metabolic disorders. The above factors may lead to the abnormal physiological function of the hypothalamic-pituitary-ovarian (HPO) axis, resulting in the disorder of sex hormone levels, the decline of follicle number and follicle dysplasia, and accelerate the decline of ovarian reserve function in patients.

This case shows that PCOS and DOR have different ovarian reserves, and also reminds us that DOR can occur in PCOS patients. To this kind of population with fertility barriers, we should solve the fertility problem as soon as possible. Especially now that the three-child policy is released in China, people who want to have two or three children should do a good job in family planning. Due to the large follicular reserve in PCOS population, many people have an optimistic attitude that they can get pregnant at any time. But often such people are at risk for DOR, even higher than the general population. After PCOS has been confirmed, women at risk of DOR should be provided with pregnancy counseling and infertility treatment, so as to avoid delaying the best time of pregnancy. If PCOS is further combined

with DOR, it will increase the difficulty of pregnancy, and even patients may lose the opportunity to become mothers.

Conflict of Interest

The authors have declared that no conflict of interest exists.

Informed Consent Statement

The subject gave informed consent.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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