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*Case Report*

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**Successful Pregnancy and Live Birth Following Hormone Replacement Treatment in a Patient with POI: A Case Report and Literature Review**

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**Abstract**

*Premature ovarian insufficiency (POI) is a condition characterized by at least four months of oligo/amenorrhea and an elevated serum follicle-stimulating hormone (FSH) level exceeding 25 IU/L on two separate occasions more than four weeks apart, with an onset before the age of 40. According to European Society of Human Reproduction and Embryology (ESHRE) guidelines, POI affects 1-2% of women of reproductive age, with 90% of cases classified as idiopathic. Approximately 25% of women with idiopathic POI may experience intermittent resumption of ovarian activity. This case report presents a 29-year-old POI patient with secondary infertility who successfully conceived and delivered a healthy baby following hormone replacement therapy (HRT).*

**Introduction**

Premature Ovarian Insufficiency (POI), previously referred to as premature ovarian failure, is a condition characterized by the cessation of ovarian function before the age of 40 (1,2). According to the European Society of Human Reproduction and Embryology (ESHRE) guidelines, POI is diagnosed when a woman experiences at least four months of oligo/amenorrhea (infrequent or absent menstruation) and has elevated serum follicle-stimulating hormone (FSH) levels above 25 IU/L on two separate occasions at least four weeks apart (3). POI affects approximately 1-2% of women in their reproductive years, with around 90% of cases being idiopathic, meaning the cause is unknown. Despite the condition's challenges, approximately 25% of women with idiopathic POI may experience intermittent resumption of ovarian activity, leading to occasional ovulation and, in rare cases, spontaneous pregnancy(4,5).

Women diagnosed with POI often experience symptoms associated with estrogen deficiency, such as hot flashes, night sweats, vaginal dryness, osteoporosis, and an increased risk of cardiovascular diseases. The condition also significantly impacts fertility, making it one of the leading causes of secondary infertility(6). Hormone Replacement Therapy (HRT) is a commonly recommended treatment to alleviate symptoms, improve overall health, and, in some cases, restore ovarian function, thereby offering a possibility of pregnancy(7,8).

This article presents a case report of a 29-year-old woman diagnosed with POI who successfully conceived and delivered a healthy baby following sequential HRT. The case highlights the role of HRT in managing POI and its potential to facilitate spontaneous pregnancy. Additionally, a review of existing literature is provided to explore the underlying mechanisms, treatment options, and outcomes related to POI and fertility restoration.

## Case Report

A 29-year-old female patient with a known history of POI and secondary infertility was evaluated. Her karyotype was confirmed as 46XX. Upon diagnosis, her hormonal profile indicated significantly elevated levels of FSH (40.55 mIU/mL) and luteinizing hormone (LH) (65.59 mIU/mL). The patient had previously experienced two spontaneous pregnancies in 2020, both of which resulted in missed miscarriages at 8 and 6 weeks, respectively.

A full recurrent pregnancy loss (RPL) evaluation was conducted, including:

- **Endocrine assessment:** Thyroid-stimulating hormone (TSH), anti-thyroid peroxidase (Anti-TPO) antibodies, prolactin, and hemoglobin A1C (HbA1c)
- **Immunological markers:** Anti-phospholipid antibodies, lupus anticoagulant,  $\beta$ 2-glycoprotein, fasting homocysteine, protein C, and protein S
- **Uterine anatomy assessment:** 3D imaging of the uterine cavity

All results were normal.

## Treatment Protocol

The patient was started on sequential HRT. The treatment regimen included:

1. Oral estradiol valerate (2 mg) for two weeks
2. Oral progesterone supplementation in the third week

Following HRT initiation, withdrawal bleeding was observed. However, subsequent hormonal assessments showed further elevations in FSH (101 mIU/mL) and LH (35.61 mIU/mL) with low estradiol ( $E_2 = 10.79$  pg/mL), suggesting persistent ovarian insufficiency.

Given the prognosis, the couple was advised on the possibility of oocyte adoption. However, during the second cycle of sequential HRT, the patient did not experience withdrawal bleeding for two months. A serum beta-human chorionic gonadotropin ( $\beta$ -hCG) test later confirmed pregnancy.

## Pregnancy Outcome

On November 2, 2022, ultrasonography confirmed an intrauterine pregnancy with a normally developed gestational sac and a crown-rump length (CRL) consistent with an 8-week fetus. Fetal heart sounds (FHS) were positive. The patient was referred to a higher obstetric unit at 10 weeks for continued antenatal care.

On July 5, 2023, the patient delivered a healthy baby girl weighing 3,460 g at full term via lower segment cesarean section (LSCS). The postpartum period was uneventful.

## Discussion

POI leads to infertility due to ovarian follicle depletion and estrogen deficiency(9). HRT is recommended for managing symptoms and preventing chronic conditions such as osteoporosis and cardiovascular disease(10). While exogenous estrogen therapy primarily alleviates symptoms, it may also improve ovarian function by enhancing granulosa cell sensitivity to FSH, potentially leading to ovulation.

Although rare, spontaneous ovulation and pregnancy can occur in POI patients. HRT can facilitate endometrial receptivity, thereby increasing the likelihood of implantation if ovulation occurs(11). This case highlights the potential for spontaneous conception and live birth in POI patients receiving HRT, emphasizing the importance of personalized fertility counseling(12,13).

## Conclusion

This case demonstrates that women with POI should be informed about the small but real possibility of spontaneous ovulation and pregnancy following HRT. While oocyte donation remains the primary fertility option, selected cases may achieve successful conception and live birth with appropriate hormonal support. Furthermore, this case reinforces the role of HRT in not only managing POI symptoms but also enhancing fertility outcomes.

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