

Successful Pregnancy in a PCOS Patient with Elevated Basal Luteinizing Hormone and Repeated Ovulation Induction Failures: A Case Report

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Abstract: Polycystic ovary syndrome (PCOS) is a multifactorial endocrine disorder characterized by chronic anovulation, hyperandrogenism, and polycystic ovarian morphology, leading to infertility. Elevated basal luteinizing hormone (bLH) levels in PCOS can impede the efficacy of ovulation induction (OI). This case report explores the management of a 26-year-old woman with PCOS and high bLH levels who experienced repeated failure in OI attempts. During in vitro fertilization-embryo transfer (IVF-ET) treatments, she underwent two cycles of controlled ovarian stimulation using long-acting gonadotropin-releasing hormone (GnRH) agonist and GnRH antagonist protocols respectively, both of which failed due to inadequate ovarian response despite normal bLH levels on the day of gonadotropin initiation. In the third cycle, a progestin-primed ovarian stimulation (PPOS) protocol combined with letrozole was adopted without bLH pretreatment, resulting in a successful pregnancy and healthy child after frozen-thawed embryo transfer. This case highlights the need for tailored approaches in managing PCOS patients with high bLH levels and indicates that elevated bLH may not always impair IVF outcomes. Further research is needed to establish the optimal bLH threshold and management protocols to enhance reproductive outcomes for these patients.

Plain Language Summary: In this case report, we share the story of a young woman with polycystic ovary syndrome (PCOS) and high basal luteinizing hormone (bLH) who was struggling with primary infertility. She has experienced multiple failed attempts on ovulation induction. During two consecutive IVF treatments, she encountered cycle cancellation due to inadequate ovarian response despite normalizing basal LH levels. In the third cycle, a progestin-primed ovarian stimulation protocol combined with letrozole was used without pretreating elevated bLH. The patient responded well to this approach and achieved a successful pregnancy, eventually giving birth to a healthy child. This case sheds light on the management of PCOS patients with high bLH levels and repeated treatment failures. It indicates that high bLH does not always compromise IVF success and inspires hope for those facing comparable challenges.

Keywords: polycystic ovary syndrome, basal luteinizing hormone, controlled ovarian stimulation, in vitro fertilization-embryo transfer

Introduction

Polycystic ovary syndrome (PCOS) is a common endocrine disorder characterized by chronic anovulation, hyperandrogenism, and polycystic ovarian morphology, affecting approximately 11–13% of women globally.¹ The underlying etiology is multifactorial, with hyperandrogenism and insulin resistance representing two key pathogenic drivers. Besides, neuroendocrine disturbance, marked by an elevated basal luteinizing hormone (bLH) level or LH/ follicle-stimulating hormone (FSH) ratio in a majority of PCOS patients, was thought to be the central mechanism of the

syndrome.² While ovulation induction (OI) is an essential approach to manage anovulation-related infertility in PCOS patients,³ these neuroendocrine disturbances may unexpectedly increase the risk of poor ovarian response (POR) during OI.⁴ Defined as diminished oocyte retrieval, increased cycle cancellation rates, and reduced clinical pregnancy rates following standard ovarian stimulation protocols, POR remains a significant challenge in approximately 5–35% of assisted reproductive technology (ART) cycles.^{5,6} The condition arises from diverse etiological factors including environmental exposures such as air pollutants and endocrine-disrupting chemicals, biological determinants like genetic predisposition and endometriosis, as well as iatrogenic causes including previous pelvic surgery or exposure to chemotherapy and radiotherapy.^{7,8} Previous studies have indicated that elevated bLH levels may be associated with suboptimal response to OI and a reduced success rate of in vitro fertilization-embryo transfer (IVF-ET) treatments.⁹ However, recent studies suggest that elevated bLH levels do not significantly influence IVF outcomes, such as the number of oocytes retrieved, the proportion of high-quality embryos, the cumulative clinical pregnancy rate, and the live birth rate.^{10,11} Therefore, the ideal approach to managing elevated bLH levels in patients with PCOS undergoing IVF/intracytoplasmic sperm injection (ICSI), as well as identifying the specific bLH thresholds required to elicit an optimal ovarian response and achieve favorable IVF outcomes, remains an issue of controversy within the clinical and research communities.

In this case report, we present a case of a 26-year-old nulligravid woman with PCOS and elevated bLH levels, who had previously experienced multiple failed OI cycles. During the controlled ovarian stimulation (COS) in IVF treatment, the patient was consecutively managed with the long-acting gonadotropin-releasing hormone (GnRH) agonist protocol and the GnRH antagonist protocol. While conventional LH suppression failed to prevent cycle cancellation due to POR, subsequent use of a progestin-primed ovarian stimulation (PPOS) protocol with letrozole (LET) (without prior LH suppression) achieved favorable ovarian response and pregnancy. This case offers novel clinical insights for managing PCOS patients with elevated bLH and prior OI failures, particularly regarding LH control and stimulation protocol selection.

Case Presentation

The Patient

A 26-year-old nulligravid woman presented to our reproductive medicine clinic in July 2021 with a history of infertility for 3 years despite regular unprotected intercourse. She had regular menstrual cycles, ranging from 25 to 35 days, and was diagnosed as PCOS based on ultrasonographic findings of bilateral polycystic ovaries and anovulation. Her hormonal profile revealed consistently elevated bLH level (>10 IU/L), as well as a high LH/FSH ratio. Despite treatment with oral contraceptive pills (OCP) for several cycles, her bLH levels remained elevated, and she experienced six unsuccessful cycles of OI with LET and human menopausal gonadotropin (hMG) due to poor ovarian response. Hysterosalpingography conducted in January 2021 demonstrated right-sided tubal obstruction and left-sided tubes lifted. Her partner's semen analysis was within normal range. The couple sought assistance with IVF for infertility treatment.

Controlled Ovarian Stimulation (COS)

Prior to initiating the COS cycle, the patient underwent serum hormonal assessment on day 2 of menstrual cycle, indicating a significant increase in bLH levels (21.66 IU/L) and an elevated LH/FSH ratio (21.66/9.99). Transvaginal ultrasonography demonstrated an antral follicle count exceeding 30 at the baseline evaluation. Given the patient's substantially elevated bLH levels and poor response to previous OI treatments, a single dose of 3.75 mg of long-acting gonadotropin-releasing hormone agonist (Decapeptyl; Ferring GmbH, Germany) was administered on cycle day 2. Twenty-eight days later, the patient's hormonal profile confirmed the restoration of LH levels and LH/FSH ratio to the normal range, which was found to be 0.84 IU/L and 2.01/0.84 separately. COS was started with high-purity hMG (HP-hMG; Ferring GmbH, Germany) 225 IU daily on August 12st, 2021. However, on day 9 of gonadotropin (Gn) administration, follicular growth was significantly delayed. The dominant follicle on the right ovary was measured as 9.8 mm in diameter, whereas the largest follicle on the left ovary was found to be 7.3 mm in diameter. Considering the possibility of poor ovarian response, the HP-hMG dose was adjusted to 300 IU daily.

Nevertheless, on day 13 of Gn administration, follicular growth remained suboptimal, with the largest right-sided follicle diameter measuring 10.4 mm and the largest left-sided follicle measuring 10.7 mm. The HP-hMG dose was further increased to 375 IU daily. During the stimulation process, the patient's LH levels continued to decline, reaching 0.06 IU/L on day 13 of Gn administration. On GnD16, follicular atresia was observed, accompanied by a drop in serum LH to 0 IU/L and a decrease in estradiol (E2) levels from 534.2pg/mL to 168.52pg/mL, leading to the cancellation of the cycle.

In September 2021, the second COS cycle was initiated. Hormonal assessment on cycle day 2 revealed normal FSH (5.54 IU/L) and LH (2.45 IU/L) levels, with slightly elevated E2 levels (83.09pg/mL). We adopted the antagonist protocol, a classic regimen recommended for PCOS patients, with HP-hMG 225 IU daily starting on cycle day 2. Eight days post-administration of treatment, a significant retardation in the progression of follicular development was re-encountered. This pattern persisted even after adjusting the HP-hMG dose to 300 IU daily. On GnD13, the dominant follicles in both ovaries were 10.2 mm and 11.0 mm in diameter separately, with serum LH levels reaching 5.05 IU/L and E2 levels reaching 585.09pg/mL. On GnD14, GnRH-antagonist (Cetrorelix; Merck-Serono, Spain) 0.25 mg daily was added. Strikingly, on GnD17, there was a marked reduction in both serum LH and E2 concentrations, with the dominant follicle on the right ovary reaching a diameter of 13.3 mm and its counterpart on the left ovary attaining 13.2 mm. Following a thorough consultation with the couple, the treatment cycle was cancelled.

On November 15, 2021, after experiencing two failed COS protocols, we re-evaluated the patient's baseline endocrine profile prior to commencing the third COS therapy. The endocrine analysis showed an elevated level of LH (15.45 IU/L) and a subtle increment in E2 (78.26pg/mL) concentrations. Regarding the inadequate ovarian response during the two preceding COS cycles, we directly utilized the progestin-primed ovarian stimulation (PPOS) protocol for the third cycle without pretreatment of the bLH. To enhance the COS response and prevent premature LH surges, we combined LET 5 mg with HP-hMG 225 IU daily to start the stimulation. Excitingly, on GnD4, the largest follicles on both sides reached 0.73 cm in diameter, with additional nine follicles measuring approximately 0.6 cm in diameter. Serum LH concentrations escalated to 25.77 IU/L, while E2 levels rose to 79.29 pg/mL, an increase that may be ascribed to the LET-mediated stimulation of endogenous Gn release. Considering the slightly smaller follicle size, the HP-hMG dose was increased to 300 IU daily. The dominant follicles on both ovaries exhibited a diameter of 11.3 mm, corresponding to an average growth rate of roughly 1 mm/day. Although the rate was lower than the anticipated threshold, the follicular development demonstrated satisfactory synchrony. Therefore, the HP-hMG dose was further adjusted to 375 IU daily. Interestingly, on GnD11, the average growth rate was observed to be approximately 1.5–2 mm/day. Concurrently, serum LH levels decreased to 8.8 IU/L, and E2 levels reached 1878 pg/mL. On GnD12, the follicles met the criteria for triggering, with serum LH levels of 7.44 IU/L and E2 levels of 2580.79pg/mL. The patient received a subcutaneous injection of 250 µg recombinant human chorionic gonadotropin (Ovidrel; Merck Serono Inc, Geneva, Switzerland) on November 17, 2021. Oocyte retrieval was performed 36 hours later on November 19, yielding a total of 15 oocytes, 7 cleavage-stage embryos on day 3, including 4 high-quality embryos. Due to the PPOS protocol, all embryos were cryopreserved. Detailed clinical course of three ovarian stimulation treatment cycles was presented in [Figure 1](#).

Embryo Transfer

Embryo transfer was scheduled on March 7, 2022. Taking into consideration the patient's irregular menstrual cycles, a hormone replacement therapy was utilized for the endometrial preparation. On day 11 of administration with Estradiol valerate (Bayer AG, Leverkusen, Germany), the endometrial thickness reached 10.6 mm, with serum LH levels of 0.13 IU/L, E2 levels of 319.52pg/mL, and progesterone levels of 0.75 ng/mL. Dydrogestrone (Abbott, Illinois, United States) 20 mg per day and progesterone sustained-release vaginal gel (Merck Serono Inc., Geneva, Switzerland) 90 mg per day were added to support endometrial transformation. On March 21, 2022, two embryos (8c-1 and 8c-2) were transferred. Thirty days after embryo transfer, a singleton pregnancy was confirmed by visualization of a gestational sac on ultrasonographic examination. The patient underwent routine prenatal care without any obstetric complications and ultimately delivered a healthy male infant with a birth weight of 3300 g and an Apgar score of 10–10–10 at term via spontaneous vaginal delivery.

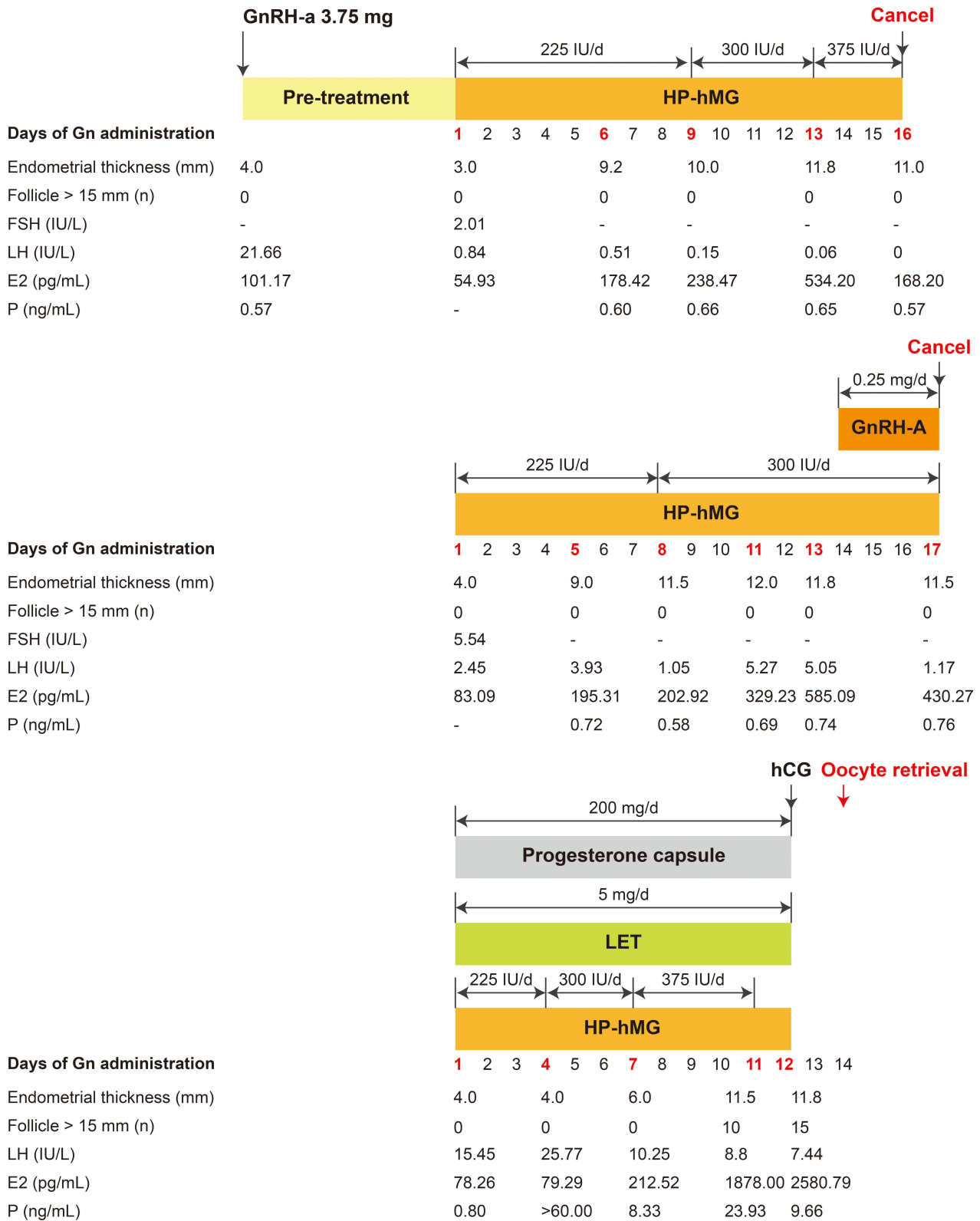


Figure 1 Detailed clinical therapy of three different ovarian stimulation treatment cycles. The color codes represent different treatment phases: yellow indicates pretreatment with GnRH-a 3.75 mg, orange denotes HP-hMG therapy, dark orange corresponds to GnRH antagonist administration, gray represents progesterone capsule treatment, and green signifies letrozole therapy. Red bold text in the “Days of Gn administration” row marks clinical visits. Arrows indicate key time points: Cycle I (Day 16) and Cycle 2 (Day 17) show cycle cancellation, while Cycle 3 includes an hCG trigger on Day 12 and oocyte retrieval on Day 14.

Abbreviations: GnRH-a, Gonadotropin-releasing hormone agonist; Gn, Gonadotropin; FSH, Follicle-stimulating hormone; LH, Luteinizing hormone; E2, Estradiol; P, Progesterone; HP-hMG, High-purity human menopausal gonadotropin; hCG, Human chorionic gonadotropin; GnRH-A, Gonadotropin releasing hormone antagonist; LET, Letrozole.

Discussion

Polycystic ovary syndrome (PCOS) is a highly heterogeneous endocrine disorder characterized by hyperandrogenism, ovulatory dysfunction, and polycystic ovaries.^{3,12} Disturbances within the neuroendocrine axis are a critical feature of PCOS patients, typically manifesting as elevated LH levels and increased LH/FSH ratios.¹³ Previous studies have elucidated that 88% of PCOS patients had elevated LH levels.¹⁴ However, the etiology of neuroendocrine dysfunction is complex, potentially involving an intricate interplay among genetic, endocrine, and metabolic determinants.¹⁵ Dapas et al analyzed biochemical and genotype data from a previously published PCOS genome-wide association study, and identified alleles in PRDM2/KAZN, IQCA1, BMPR1B/UNC5C and CDH10 loci were associated with the reproductive subtype which was characterized by higher LH and sex hormone binding globulin levels with relatively low body mass index (BMI) and insulin levels.¹⁶ Additionally, LH β (rs1056917) and lutropin receptor (rs61996318) polymorphism were found to be strongly associated with the high LH/FSH ratio in PCOS patients, as the LH/FSH ratio was significantly higher in mutant homozygous and heterozygous variants when compared with wild-type.¹⁴ Apart from hereditary factors, endocrine and metabolic dynamics play a pivotal role in the dysregulation of neuroendocrine physiology. To our knowledge, the secretion of LH and FSH is modulated by GnRH pulsatility of GnRH neurons in the hypothalamus, and kisspeptin serves as the principal regulator of GnRH secretion, while neurokinin B (NKB) and dynorphin are involved in the regulation of kisspeptin release in the kisspeptin-neurokinin B-dynorphin A neurons.¹⁷ Previous investigations have showed that PCOS patients had significantly higher serum kisspeptin levels than healthy individuals.¹⁸ LET induced PCOS-like phenotypes mouse model exhibited rapidly activated LH pulsatility *in vivo*, with increased pulse frequency, amplitude, and basal levels, accompanied by markedly elevated Kiss1, Tac2, and Pdyn expression with increased Kiss1 neuronal activation in the hypothalamic arcuate nucleus. The study suggested that increased hypothalamic kisspeptin and NKB levels may be fundamental contributors to the hyperactive LH pulse secretion in the LET-induced PCOS-like condition, and perhaps, in PCOS women.¹⁹ In addition, anti-Müllerian hormone (AMH) is directly associated with the LH/FSH ratio, a recent study illustrates that elevated AMH serum levels were correlated with increased hypothalamic activity/axonal-glia signaling in PCOS patients, uncovering a central function for AMH in the regulation of GnRH terminals and their tanycytic sheaths remodeling.²⁰ Furthermore, metabolic factors also contribute to the abnormal Gn levels in PCOS patients. Moran et al found that the LH levels and LH/FSH ratio were significantly higher in low-BMI than in high-BMI PCOS patients with the BMI cutoff value of 27 kg/m².²¹ Interestingly, Pratama et al conducted a study aiming to deepen the understanding of the metabolic disorder in 110 lean PCOS patients, and confirmed a positive correlation between dynorphin and the LH/FSH ratio, but not between kisspeptin and the LH/FSH ratio.²² In the present case, we found a persistently elevated bLH levels in the patient with normal BMI of 20.8kg/m², which was consistent with the above conclusion that a higher bLH level was more frequent in lean PCOS patients. Considering the rarely used LH polymorphism assessment, the potential involvement of genetic determinants in the observed increase of LH concentrations remains undetermined.

It is well-established that LH plays a critical role in the regulation of follicular steroidogenesis and development, as well as oocyte maturation.^{23,24} However, consensus on the ideal bLH concentration for OI or COS has not yet been obtained. Some scholars have proposed that elevated levels of LH during the follicular phase was linked with decreased oocyte quality, accelerated resumption of meiosis, and premature ovulation.²⁵ Wang et al retrospectively analyzed the data from 533 cycles of COS and intrauterine insemination (IUI) treatments from PCOS women and illustrated that hypersecretion of bLH was connected to an increased risk of pregnancy loss, since early miscarriage grew significantly while pregnancies and live births ceased to increase when bLH above 11.69 mIU/mL.⁹ What's more, an extensive array of in-depth fundamental research has been undertaken to delve into the underlying implications of high bLH concentrations on the process of pregnancy. Park et al raised that excessive LH elicited extragonadal suppression of tissue regeneration-related functions such as self-renewal, migratory capacity, multilineage differentiation potential, and pluripotency/stemness by inhibiting pro-survival Akt and ERK1/2 signaling pathways in endometrial stem cells, thus, decreasing the endometrial receptivity and posing a detrimental effect on pregnancy.²⁶ Utilizing the emerging RNA sequencing technology, Wan et al revealed that in cultured GCs, both insufficient and excessive recombinant LH treatments attenuated the activity of mitochondrial dehydrogenase, indicating that recombinant LH could directly affect

GCs at subcellular level.²⁷ Nevertheless, a subset of investigators has independently scrutinized the impact of elevated LH levels on pregnancy outcomes within the ovulation induction and IVF procedures, analyzing the effects across diverse protocols. Wang et al demonstrated that no statistically significant disparities were observed in baseline demographic characteristics and IVF outcomes, including the number of oocytes retrieved, the proportion of high-quality embryos, the cumulative clinical pregnancy rate, and the live birth rate when considering the basal serum LH levels. Additional analysis highlighted an intriguing fact that patients exhibiting a high LH level on trigger day (hLH) / basal LH (hLH/bLH) ratio (≥ 1) achieved a superior rate of high-quality embryos compared to those with an hLH/bLH ratio ranging between 0.5 and 1.0. Moreover, the cumulative clinical pregnancy rate was notably higher in the cohort with an hLH/bLH ratio ≤ 0.5 compared to the other two groups, suggesting a potential role of LH during COS on pregnancy outcomes in women with PCOS undergoing GnRH-antagonist protocol.¹⁰ Likewise, Sun et al executed a retrospective cohort study encompassing 1011 PCOS individuals treated with PPOS protocol, and the data yielded that the group with LH ≥ 10 mIU/mL showed a lower mean total hMG dose used but higher numbers of oocytes retrieved, metaphase II oocytes, embryos and top-quality embryos developed than the groups with lower basal LH levels. There were no significant differences in the rates of oocyte retrieval, fertilization, implantation, clinical pregnancy and miscarriage between the groups based on frozen embryo transfer (FET), revealing no detrimental impact of elevated bLH on the ultimate outcomes of IVF/ICSI cycles treated with hMG + Medroxyprogesterone Acetate (MPA) in women with PCOS.¹¹ Similarly, Ganor-Paz et al found that there was no difference in pregnancy rates among PCOS patients with day 3 LH/FSH ratio ≥ 1.5 undergoing IVF treatment with GnRH-agonist/antagonist protocols or in vitro maturation treatment and suggesting that high LH/FSH ratio had no adverse effects on pregnancy outcomes among three COS models.²⁸ Within the present case, a sustained elevation of bLH levels was noted, which did not demonstrate a discernible reduction following the administration of OCP. Historical records indicated that multiple OI cycles were devoid of effective follicular growth. After the implementation of a long-acting GnRH agonist during the IVF treatment, although LH concentrations were normalized, the patient exhibited an inadequate ovarian response and follicular atrophy. This scenario underscores the critical importance of optimal LH levels during the ovulation induction phase for a positive reproductive outcome, a conclusion that resonates with the research findings published by Wang et al.¹⁰ Additionally, it is still unknown whether individual patients with a high level of bLH would benefit from pre-suppression of LH. The utilization of OCP preceding ART was employed in patients with PCOS to orchestrate the timing of the treatment cycle or to inhibit endogenous LH and androgen production.^{29,30} Pan later found that successive cyclic OCP pretreated PCOS patients achieved higher implantation rate and clinical pregnancy rate.³¹ However, others argue that there is limited evidence to support the adoption of this approach and point out that the potential risks and side effects of OCP might outweigh its benefits. Fu et al found that high LH levels in PCOS were not solid evidence of poor prognosis in letrozole-induced ovulation, while elevated LH level after letrozole administration may be a prospective predictor for better OI outcomes, proposing that prohibition of LH secretion was not needed.³² Song et al performed a meta-analysis exploring the efficacy of OCP pretreatment in women with PCOS before ART, and the results implied an adverse effect on clinical outcomes, especially with GnRH antagonist protocol. Unfortunately, the present investigation failed to delineate the bLH profiles of patients with PCOS who were administered with OCP, thereby omitting an assessment of whether their bLH levels were within the normal range.³³ Xu et al aimed to elucidate whether OCP pretreatment impairs pregnancy outcomes in PCOS women undergoing GnRH agonist protocol, and found that patients in the OCP dual suppression GnRH agonist protocol group (OC-LP group) had significantly higher bLH (within the normal range), basal estradiol, and testosterone than the GnRH agonist protocol group (LP group), and serum luteinizing hormone level, endometrial thickness, and live birth rate were significantly reduced in the OC-LP group in fresh cycle.²⁵ Homminga et al revealed that thin (<8 mm) endometrial lining was more prevalent in preimplantation genetic testing for monogenic disease (PGT-M) patients compared to the regular IVF/ICSI population, which was associated with both longer prior hormonal contraceptive use and a shorter cessation interval of hormonal contraceptives before IVF/ICSI treatment, indicating that the effect of OCP on pregnancy is persistent.³⁴ Remarkably, the potential role of bLH pre-treatment may need to be evaluated in conjunction with basal AMH levels. Basal AMH level serves as a valuable biomarker for predicting both suboptimal and excessive ovarian responses during IVF stimulation, facilitating tailored ovarian stimulation strategies.³⁵ Existing literature establishes reference ranges that contextualize our patient's profile: Li et al reported a median AMH

level of 3.888 ng/mL in healthy 26-year-old women,³⁶ while another study identified similar ranges (50th percentile: 4.35 ng/mL).³⁷ Based on Li's study, the cut-off value of multiple of the median AMH level for diagnosing PCOS was 1.5 at the fixed specificity of 80% and the corresponding sensitivity of 73%.³⁶ Although our patient's AMH (3.85 ng/mL) fell within the normal range for healthy women, it was comparatively low for PCOS patients, potentially indicating possible ovarian reserve compromise in this specific clinical context. This created a unique clinical challenge. While elevated bLH in PCOS often necessitates suppression, excessive LH reduction in patients with borderline reserve (as indicated by AMH) risks may compromise ovarian response. This case highlights the challenges of managing PCOS patients with elevated bLH levels who have experienced multiple unsuccessful OI. The patient's initial response to COS was poor, despite the use of different protocols and adjustments in gonadotropin doses. The persistent elevation of bLH levels despite the use of oral contraceptives was a significant concern. The GnRH antagonist protocol utilized in the second COS cycle resulted in a poor and slow ovarian response, mainly attributed to the attenuated LH levels during the COS phase, which was consistent with the findings from Gao's study that OCP pretreatment prior to antagonist therapy in PCOS patients not only escalated the dosages of gonadotropins administered during the ovulation induction phase but also failed to ameliorate pregnancy outcomes.³⁸ PPOS protocol employed in the third IVF cycle proved to be effective for this patient. High concentration of progesterone effectively prevented an LH surge and the addition of letrozole to the PPOS protocol further improved the ovarian response. The use of high doses of hMG and careful monitoring of the patient's hormonal profile allowed for successful oocyte retrieval and embryo development, highlighting the need for AMH-stratified LH management in PCOS.

An increased probability of early LH surge is a concern that warrants attention in women with PCOS, particularly among those with high BMI.³⁹ Early LH surge is related to premature ovulation and luteinization of follicles, which can affect the number of retrieved oocytes, oocyte and embryo quality, and endometrial receptivity. Previous studies have demonstrated that severe LH suppression is detrimental to patients undergoing IVF treatment, Luo et al highlighted a low LH level (<1.5mIU/mL) on the COS initiation day was associated with adverse ART outcomes, including fewer oocytes, higher early pregnancy loss rate (ePLR) and lower live-birth rate (LBR) in fresh embryo transfer cycle and lower cumulative clinical pregnancy rate (CPR) and LBR in the entire ovarian-stimulation cycle. Besides, LH on the COS initiation day was an independent factor affecting ePLR after multivariate regression.⁴⁰

Therefore, it is of great significance to select an optimal COS protocol to balance the follicular development and prevention of early LH surge in such patients from the perspective of bLH levels. As reported in the present case, the precipitous decrease or prolonged state of LH suppression during the COS may have adversely affected follicular development although no premature LH surge occurred in either the GnRH agonist or antagonist protocols, which was consistent with the perspectives mentioned above. For the third COS cycle, we utilized standard PPOS protocol combined with LET, and a transient elevation of LH levels on day 4 of Gn administration was observed followed by incrementally decreasing to 10 IU/L. Encouragingly, the patient exhibited a robust response to PPOS protocol, and she ultimately achieved a successful pregnancy and delivered a healthy child after a FET cycle.

Conclusion

In conclusion, for PCOS patients with elevated bLH levels, the presence of excessively low LH levels or rapid LH decline during COS poses a risk of suboptimal ovarian response. In GnRH-a cycles, profound pituitary suppression creates an extremely low LH environment that may compromise follicular development in PCOS patients with inherently elevated bLH, while GnRH antagonist protocols induce rapid LH decline after initiation, potentially causing insufficient late follicular phase support. In the current case, higher bLH levels did not impair the efficacy and outcomes of IVF treatments with PPOS protocol. The PPOS protocol demonstrates a moderate reduction in LH levels throughout the COS phase, potentially offering a therapeutic advantage to individuals with PCOS characterized by elevated bLH levels. Further research is warranted to elucidate the optimal bLH threshold and the corresponding management protocols for such patients and improve their reproductive outcomes during IVF treatment.

Abbreviations

PCOS, polycystic ovary syndrome; bLH, basal luteinizing hormone; FSH, follicle-stimulating hormone; OI, ovulation induction; POR, poor ovarian response; ART, assisted reproductive technology; IVF-ET, in vitro fertilization-embryo transfer; ICSI, intracytoplasmic sperm injection; COS, controlled ovarian stimulation; GnRH, gonadotropin-releasing hormone; PPOS, progestin-primed ovarian stimulation; LET, letrozole; OCP, oral contraceptive pills; hMG, human menopausal gonadotropin; HP-hMG, high-purity hMG; Gn, gonadotropin; E₂, estradiol; BMI, body mass index; neurokinin B, NKB; AMH, anti-Müllerian hormone; IUI, intrauterine insemination; AFC, antral follicle count; hLH, LH level on trigger day; FET, frozen-thawed embryo transfer; MPA, medroxyprogesterone acetate; PGT-M, preimplantation genetic testing for monogenic disease; ePLR, early pregnancy loss rate; LBR, live-birth rate; CPR, clinical pregnancy rate.

Data Sharing Statement

Please contact the corresponding author Xiaokui Yang for data requests.

Ethics Approval and Consent to Participate

This case report was reviewed and approved by the Ethics Committee of the Beijing Obstetrics and Gynecology Hospital, Capital Medical University, 2018-KY-015-01. Written informed consent was obtained from the participant.

Consent for Publication

Written informed consent was provided from the patient for publication.

Author Contributions

Yu Liang and Xiaokui Yang are co-corresponding authors who contributed equally to this work. All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors report no conflicts of interest in this work.

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