International Medical Case Reports Journal

Dovepress
Taylor & Francis Group

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CASE SERIES

Platelet-Rich Plasma Therapy in Premature Ovarian Insufficiency: A Case Series of IVF Outcomes

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Introduction: Premature ovarian insufficiency (POI) leads to the early loss of ovarian function before age 40, resulting in infertility and hormonal imbalance. Despite the use of assisted reproductive technologies (ART), success rates remain low in this population. Platelet-rich plasma (PRP) therapy is emerging as a potential adjunct to enhance ovarian reserve.

Case Illustration:

Case 1: A 25-year-old nulliparous woman with a history of ectopic pregnancy and an anti-Müllerian hormone (AMH) level below 1 ng/mL received two PRP injections scheduled between days 7 to 12 of her cycle. After the first injection, her AMH level remained <0.5 ng/mL. Following the second PRP injection, her AMH level increased to >0.5 ng/mL. A frozen embryo transfer resulted in a successful term pregnancy and healthy newborn.

Case 2: A 36-year-old nulliparous woman, married for seven years, also presented POI and AMH levels <1 ng/mL followed the same PRP and IVF protocol. After two PRP sessions, her AMH levels improved similarly to Case 1. Despite an initial pregnancy, the patient experienced pregnancy loss.

Conclusion: These findings suggest that PRP may improve ovarian response in women with POI undergoing IVF. Further studies are warranted.

Keywords: in vitro fertilization, IVF (D005307), infertility (D007246), platelet-rich plasma, PRP (D053657), primary ovarian insufficiency, POI (D016649)

Introduction

Infertility, defined as the inability to conceive following 12 months of consistent unprotected sexual activity, affects approximately 15% of couples worldwide and can lead to significant psychological and social consequences.[1] The World Health Organization (WHO) reports that female infertility accounts for 37% of cases, male factors 8%, and both partners in 35%. Among women, ovulatory disorders, endometriosis, pelvic adhesions, tubal blockages, and hyperprolactinemia are frequent causes.[2]

The European Society of Human Reproduction and Embryology (ESHRE) defines primary ovarian insufficiency (POI) refers to the loss of ovarian function before age 40, characterized by menstrual disturbances (amenorrhea or oligomenorrhea for at least 4 months) and persistently elevated follicle-stimulating hormone (FSH) levels (>25 IU/L on two occasions at least 4 weeks apart).[3,4] Unlike menopause, POI may allow intermittent ovulation. The prevalence of POI rises with age, affecting approximately 1% of women by age 40. POI may be spontaneous or induced by medical interventions such as surgery, chemotherapy, or radiation.

Ovarian failure can be classified as primary, due to intrinsic ovarian dysfunction (eg, surgical removal, hereditary disorders), or secondary, due to disruption in hormonal signalling from the hypothalamus or pituitary gland.[5] Management guidelines from ESHRE) guidelines, emphasise a comprehensive, multidisciplinary approach to POI, including hormone replacement therapy (HRT) until the average age of natural menopause, fertility counselling, and monitoring for long-term health risks.[3,4]

Despite various assisted reproductive technology (ART) methods, a significant proportion of embryo implantation attempts remain unsuccessful. Platelet-rich plasma (PRP) therapy is emerging as a promising adjunct treatment for

Received: 20 March 2025
Accepted: 27 June 2025
Published: 8 July 2025

patients with diminished ovarian reserve, including those with POI. Derived from autologous blood with platelet concentrations 4–5 times higher than baseline, PRP contains multiple cytokines and growth factors such as vascular endothelial growth factor (VEGF), transforming growth factor (TGF), platelet-derived growth factor (PDGF), and epidermal growth factor (EGF), which may stimulate ovarian tissue regeneration and improve ovarian function.[6]

Current guidelines for the management of in vitro fertilization (IVF) and embryo transfer focus on maximizing success rates while minimizing risks such as multiple pregnancies and ovarian hyperstimulation syndrome (OHSS). PRP has been investigated not only for ovarian rejuvenation but also for improving endometrial thickness and implantation rates in cases of thin endometrium. Early studies suggest PRP enhances pregnancy outcomes by promoting a more receptive uterine environment.[6]

This case series evaluates the effects of intraovarian PRP therapy on ovarian reserve markers and pregnancy outcomes in two women diagnosed with POI undergoing in vitro fertilization (IVF).

Case Illustration

Patient Selection and PRP Preparation

This case series illustrates two patients with a history of infertility who underwent intraovarian PRP therapy followed by IVF. Both patients included in this case series fulfilled the diagnostic criteria for POI as defined by the ESHRE. These criteria include: age under 40 years, menstrual disturbance (oligomenorrhea or amenorrhea) for at least four months, and elevated follicle-stimulating hormone (FSH) levels >25 IU/L on at least two occasions. In both cases, AMH levels were significantly reduced (<1 ng/mL), and antral follicle count (AFC) was low. Neither patient had undergone bilateral oophorectomy nor had a history of exposure to gonadotoxic agents. Patients were selected for intraovarian PRP therapy based on spontaneous POI diagnosis, absence of identifiable secondary causes such as autoimmune disorders or chromosomal abnormalities, and their eligibility for IVF. Individuals with POI due to surgical causes, prior chemotherapy or radiotherapy, active pelvic infection, or uterine anomalies were excluded.

PRP was prepared using the T-Lab autologous kit, involving 20–60 mL peripheral blood centrifuged to yield 4–8 mL PRP with platelet concentrations around 900,000/µL. PRP was injected intraovarian under sedation, 2–4 mL per ovary, administered twice per patient with sessions spaced one month apart. The PRP was used within two hours of preparation.

Case 1

Patient Characteristics

A 25-year-old nulliparous woman with a history of ectopic pregnancy in 2021 and right salpingectomy presented to our IVF clinic with infertility concerns. Physical examination was normal, with a BMI of 25.53 kg/m². Initial laboratory tests indicated low AMH at 0.36 ng/mL (normal range: 1.0–4.0 ng/mL), elevated FSH at 13.3 mIU/mL (normal range for Day 2–3 of the menstrual cycle: 2.5–10.2 mIU/mL), and low luteinizing hormone (LH) at 2.48 mIU/mL (normal range: 1.9–12.5 mIU/mL). Transvaginal ultrasound performed on the second day of menstruation revealed an AFC of 2, with one follicle in each ovary (normal range for good ovarian reserve: 6–10 follicles per ovary). Hysterosalpingography indicated a non-patent right tube but a patent left tube. The husband's semen analysis indicated teratozoospermia. Despite her regular menstrual history, her low AMH, high FSH, and low AFC indicated diminished ovarian reserve, meeting the criteria for POI per ESHRE guidelines. Consequently, ovarian PRP therapy was considered before IVF to enhance her ovarian response.[5]

PRP Intervention

The PRP was prepared using a T-Lab autologous platelet-rich plasma kit. Peripheral blood volumes of 40–60 mL were drawn per session, yielding 6–8 mL of PRP after centrifugation and extraction from the buffy coat layer. The platelet concentration was approximately 900,000/µL. Intraovarian PRP injections were administered under conscious sedation, with 2–4 mL injected per ovary. The patient underwent two PRP sessions spaced one month apart. After the first session, AMH increased to 0.46 ng/mL, FSH rose to 18.09 mIU/mL, and LH increased to 3.23 mIU/mL. Following the second session, AMH further increased to 0.63 ng/mL, and FSH decreased to 2.63 mIU/mL. PRP was prepared fresh for each session, using 20 mL of peripheral blood per procedure, with injections performed within two hours of preparation to maintain viability.

IVF Outcome

Patient received growth hormone, DHEA, folic acid, and vitamin D3 for 3 months before IVF stimulation. Controlled ovarian stimulation began on the third day of menstruation with clomiphene citrate for five days, followed by recombinant FSH (300 IU) and LH (150 IU). Cetrorelix acetate (0.25 mg) was administered from day 8. Growth hormone was continued daily until oocyte retrieval. Four oocytes were retrieved from four follicles, yielding one high-quality blastocyst that was cryopreserved. A frozen embryo transfer performed on August 6, 2023, resulted in a positive beta-hCG (547.26 mIU/mL) and ultrasound-confirmed fetal heartbeat, culminating in a successful pregnancy and live birth. Figures 1 and 2 shows an IVF Stimulation Chart Case 1. Figure 3 showed a blastocyst embryo was on good quality in case 1.

Case 2

Patient Characteristics

A 36-year-old nulliparous woman, married for seven years, presented with infertility. Her physical examination was normal, with a BMI of 27.38 kg/m². Laboratory evaluation revealed a low AMH of 0.25 ng/mL, elevated FSH of 18.52 mIU/mL, and low LH of 1.88 mIU/mL. Hysterosalpingography demonstrated bilateral tubal blockage. Transvaginal ultrasound on day 2 of menstruation showed an AFC of 3 (one follicle in the right ovary, two in the left), below the normal range of 6–10 follicles per ovary. The husband's semen analysis indicated severe oligoteratozoospermia. The patient's hormonal profile and ultrasound findings met the ESHRE diagnostic criteria for POI, characterized by hypergonadotropic hypogonadism. Given her history of regular menstruation earlier in life, secondary amenorrhea consistent with POI was diagnosed.

PRP Intervention

The patient received two ovarian PRP treatments administered between days 7 and 12 of the menstrual cycle. Each session involved drawing 20 mL of peripheral blood, centrifuged for 15 to 30 minutes to yield 4 mL of PRP from 10 mL of blood. The PRP was injected intraovarian within two hours of preparation. Following the first PRP treatment, AMH improved to 0.65 ng/mL, FSH decreased to 15.26 mIU/mL, and LH increased to 4.89 mIU/mL. After the second session, AMH rose further to 0.71 ng/mL, and FSH decreased to 8.52 mIU/mL.

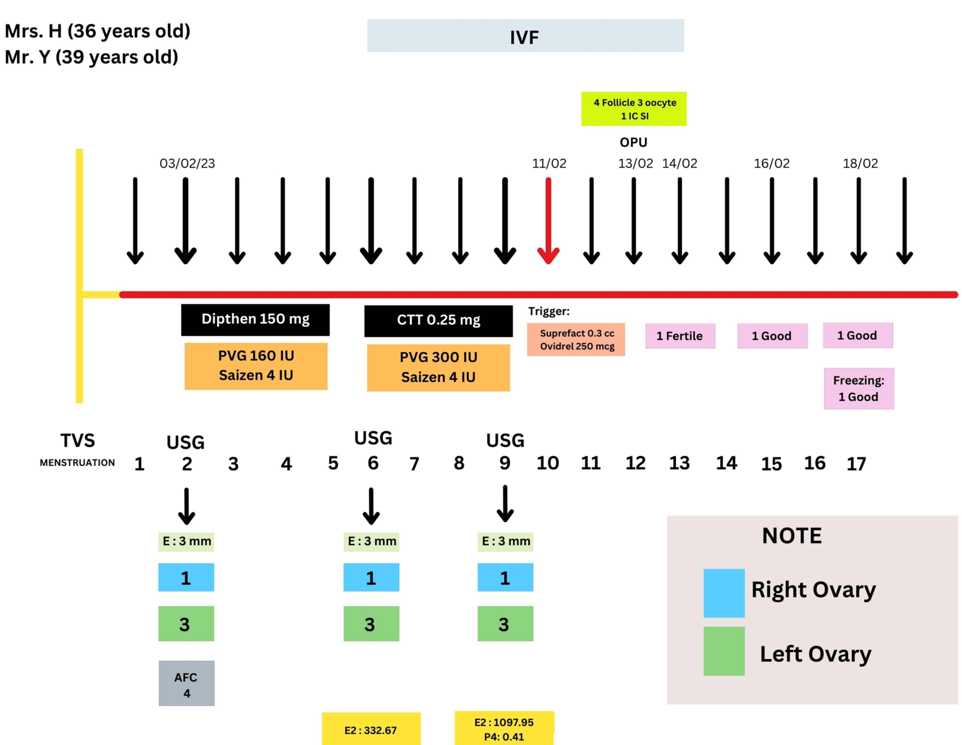

Figure 1 IVF Stimulation Chart Case 1.

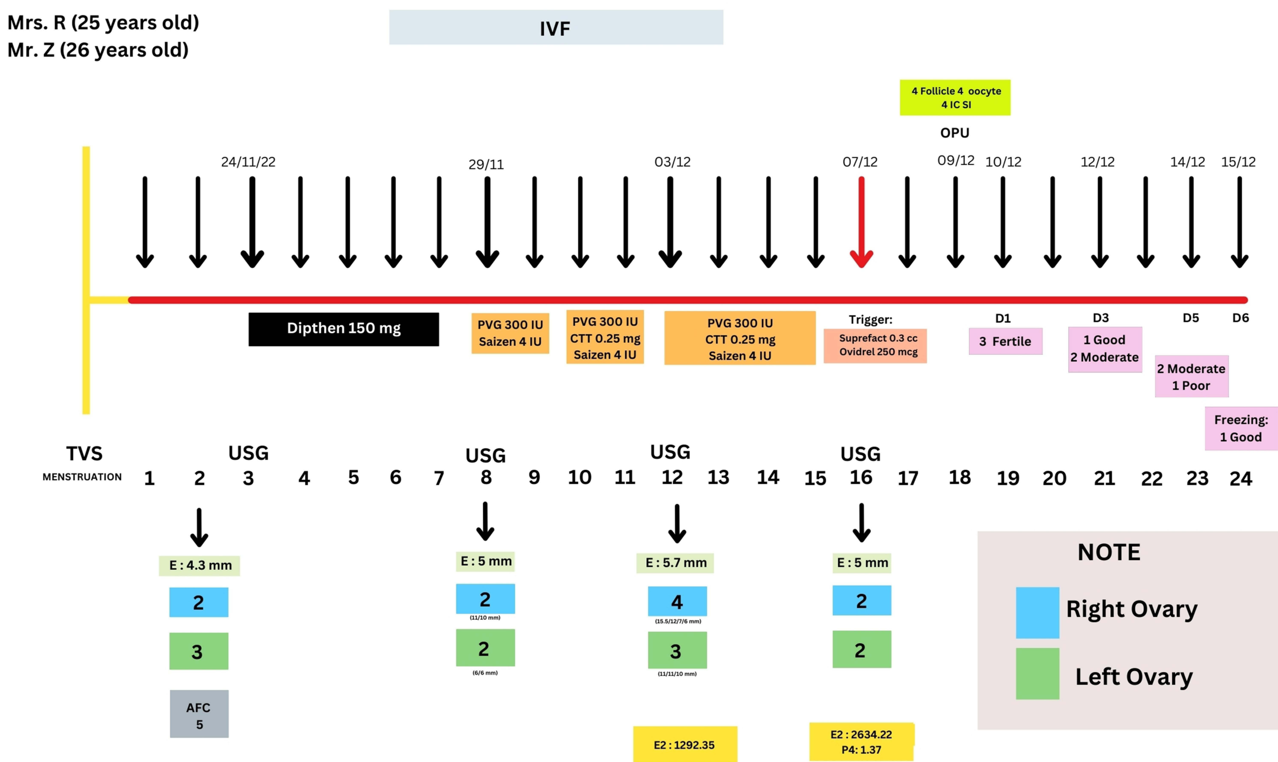

Figure 2 The Frozen-embryo-transfer (FET) chart Case 1.

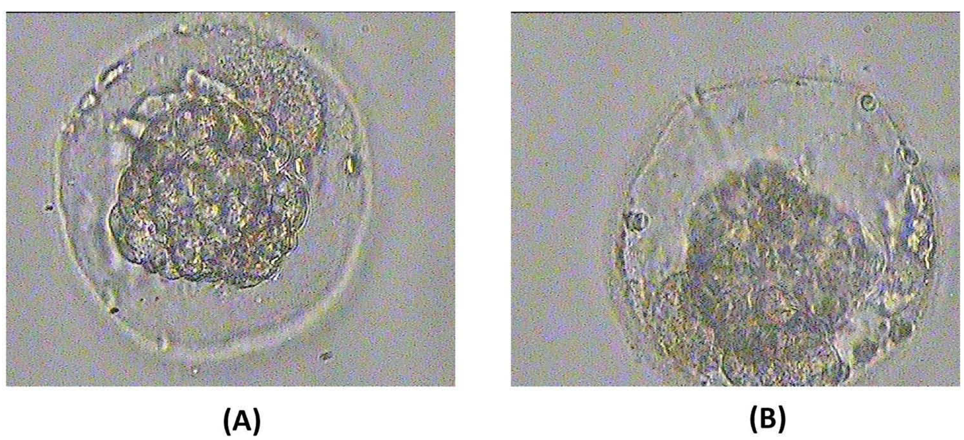

Figure 3 The blastocyst embryo was on good quality in the first case-patient (**A**) thawing (**B**) assisted hatching.

IVF Outcome

Patient received growth hormone, DHEA, folic acid, and vitamin D3 for 3 months before IVF stimulation. Controlled ovarian stimulation began on the second day of menstruation with clomiphene citrate for five days, followed by recombinant FSH (300 IU) and LH (150 IU). Cetrorelix acetate (0.25 mg) was given starting day 7. Growth hormone administration continued daily until oocyte retrieval. Three oocytes were collected from four follicles, resulting in one high-quality blastocyst that was frozen. Frozen embryo transfer on May 31, 2023, led to a positive beta-hCG (187.08 mIU/mL) and confirmed fetal heartbeat on ultrasound, though the patient later experienced early pregnancy loss. Figures 4 and 5 shows the Frozen-embryo-transfer (FET) chart while Figure 6 shows a blastocyst embryo was on good quality in case 2.

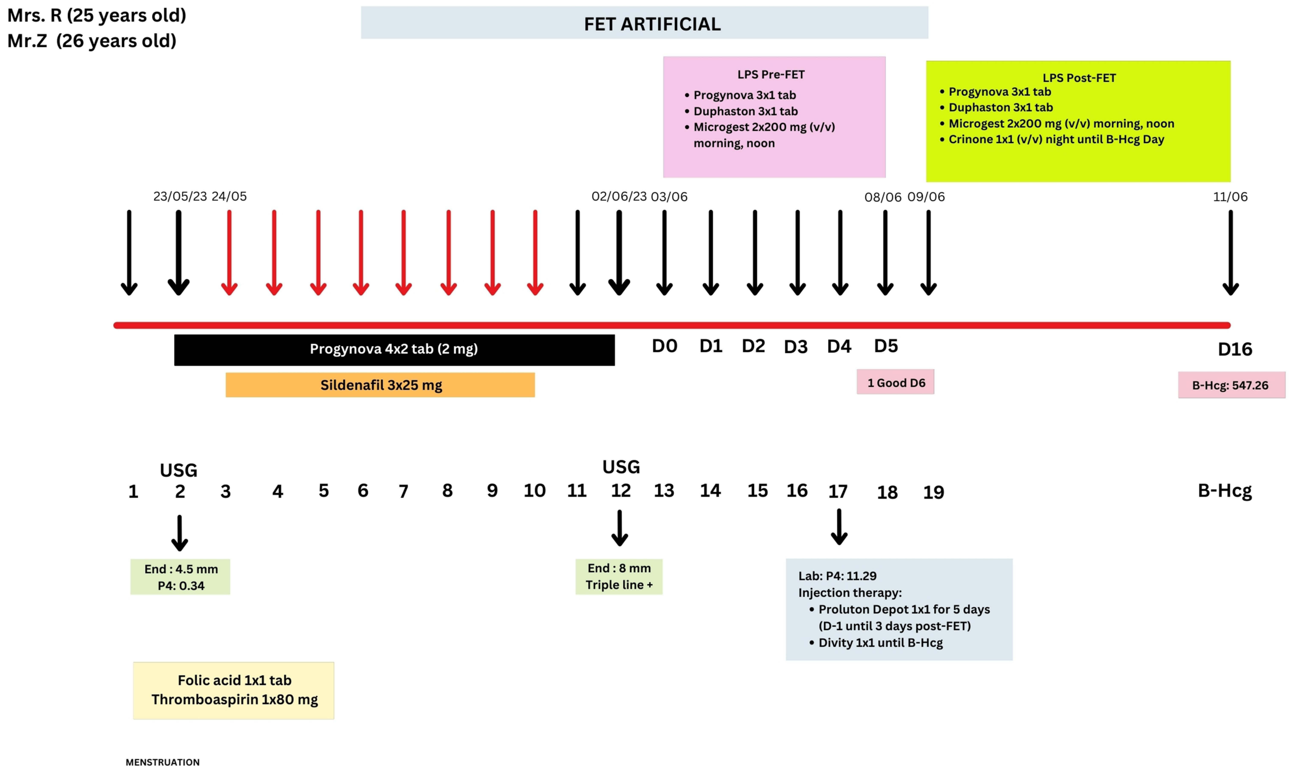

Figure 4 The Frozen-embryo-transfer (FET) chart Case.

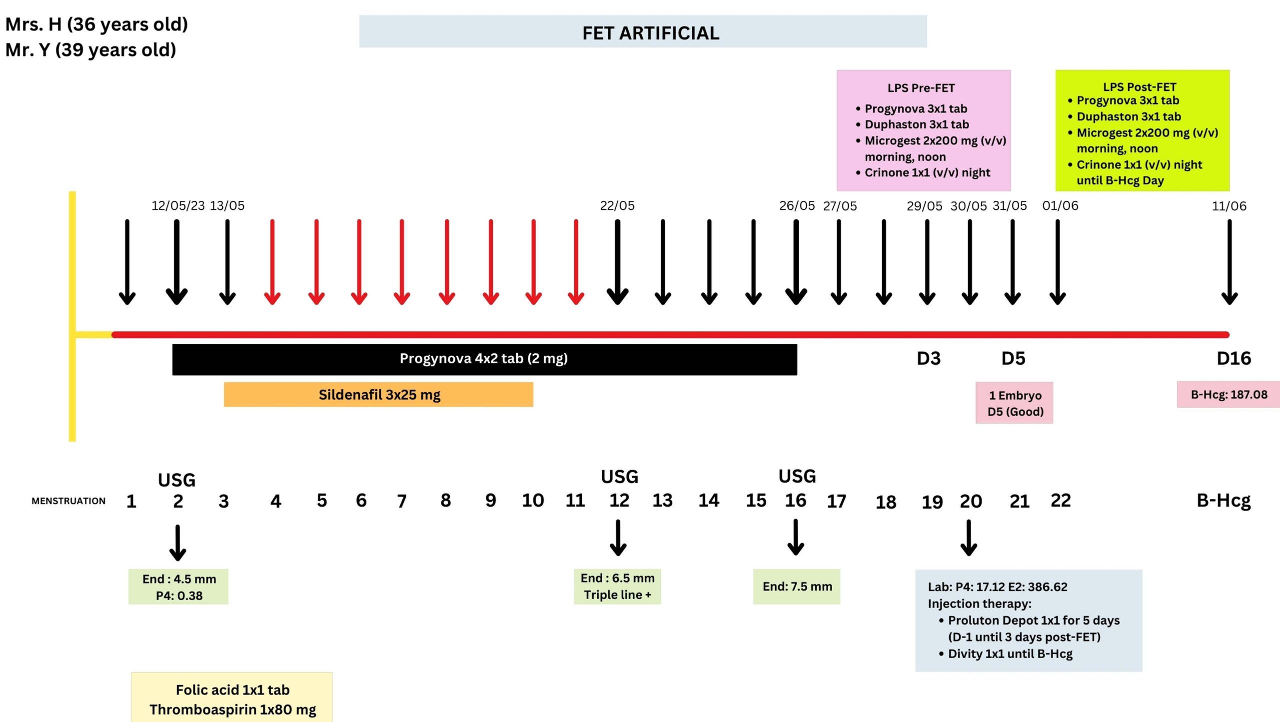

Figure 5 IVF Stimulation Chart Case 2.

https://doi.org/10.2147/IMCRJ.S527318

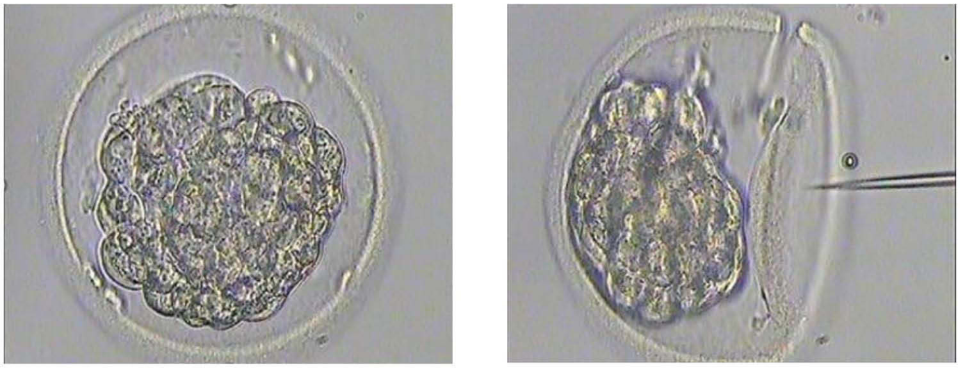

Figure 6 The blastocyst embryo was on good quality in the second case-patient (**A**) thawing (**B**) assisted hatching.

Discussion

POI affects 10–28% of cases primary amenorrhea and 4–18% of secondary amenorrhea, with significant psychological as well as physical impacts on affected women.[7] Premature ovarian insufficiency (POI) is marked by disrupted folliculogenesis, which may present as a decreased follicle pool, increased follicular atresia, or defective recruitment mechanisms. These abnormalities contribute to a significantly reduced ovarian reserve and are a major cause of infertility in affected individuals.[7–9]

The pregnancy rate in POI patients remains low (5–10%), despite advances in reproductive technologies, and traditional treatments such as ovarian stimulation protocols, androgen supplementation, and novel approaches like stem cell therapy or ovarian tissue autotransplantation have shown limited success. Recently, autologous platelet-rich plasma (PRP) ovarian injections have emerged as a promising therapeutic approach. PRP, rich in growth factors and cytokines such as VEGF, IGF, PDGF, and TGF-β, promotes angiogenesis, tissue regeneration, and cellular proliferation, potentially rejuvenating ovarian tissue and improving function.[3] Concentrating cytokines and growth factors in PRP and injecting them directly into ovarian tissue is expected to improve ovarian function. Several prior studies reported increased ovarian angiogenesis, folliculogenesis, improved menstrual cycles, and improved ovarian function after PRP injection.[3] Several studies have evaluated autologous PRP as proven to increase success in some cases of infertility.[10–12]

In this report, we present two cases of POI patients treated with repeated intraovarian PRP injections followed by IVF stimulation. Both patients underwent standardized controlled ovarian stimulation protocols after PRP therapy, leading to the retrieval of oocytes, successful blastocyst formation, and positive pregnancy outcomes. Our findings align with previous studies demonstrating PRP's potential to increase AMH levels, reduce FSH, enhance folliculogenesis, and improve pregnancy rates in women with diminished ovarian reserve (DOR).[13,14]

Treatment Approaches

Autologous PRP is derived by drawing a person's blood from a peripheral vein, which is then centrifuged to eliminate red blood cells. This process aims to produce a concentrated platelet sample with growth factor levels 5 to 10 times higher than those released by activated platelets. The typical PRP preparation involves collecting whole blood, an initial centrifugation to separate and remove red blood cells, followed by another centrifugation to concentrate the platelets, and finally, adding a platelet agonist to activate the sample.[11,15]

A post-PRP assessment was conducted to evaluate the parameters of AMH, FSH, and AFC. Stimulation is performed for the IVF program if it shows improvement. Following Farimani et al's research involving 19 participants, it was found that the average number of oocytes before and after PRP injection was 0.64 and 2.1 respectively. Two patients experienced spontaneous pregnancy. The third case achieved clinical pregnancy and delivered a healthy baby. In cases of difficulty getting pregnant due to ovarian dysfunction, action is taken to inject PRP into both ovaries. The effect of PRP is increasing the number of ovarian oocytes, especially in women with poor ovarian reserve and POI, autologous intraovarian PRP therapy increases AMH levels and decreases FSH concentrations, with a trend of increasing live birth rates.[16]

Similar effects were also found in women with chronic endometritis and recurrent implantation failure. Case of a 35-year-old woman with POI, six failed attempts after embryo transfer. The patient underwent FET of two blastocysts and succeeded in getting pregnant with twins. Four weeks after a positive β-hCG pregnancy test, clinical pregnancy was confirmed by observing fetal cardiac activity on transvaginal ultrasound. Twins were born at 36 weeks gestation with body weights of 2.28 kg and 2.18 kg.[17]

PRP comprises many growth factors involved in the pathophysiology of ligament restoration, including VEGF, IGF-I, PDGF, hepatocyte growth factor (HGF), Transforming Growth Factor Beta (TGF-β), and Fibroblast Growth Factor (FGF).[18] The primary benefits associated with the utilization of platelet-rich plasma (PRP) include its inherent autologous properties, absence of immunological responses and potential transmission of germs from the donor, its straightforward and expeditious preparation process (about 30 minutes from blood collection to application), and its cost-effectiveness However, it's important to note that PRP therapy is contraindicated for patients with coagulation abnormalities, breastfeeding or pregnant women, individuals with cancer, active infections, and those on long-term use of non-steroidal anti-inflammatory drugs (NSAIDs).[17]

In a prospective study by Cakiroglu et al, intraovarian injection of autologous platelet-rich plasma (PRP) was found to enhance ovarian response to stimulation and improve in vitro fertilization (IVF) outcomes in women diagnosed with primary ovarian insufficiency (POI). In this cohort, following PRP administration, 23 women (7.4%) achieved spontaneous conception, 201 women (64.8%) developed antral follicles and proceeded to IVF, while 87 women (27.8%) did not form antral follicles and, thus, received no further intervention. However, this study utilized only a single PRP injection without any follow-up interventions until conception was achieved.[19]

The current study builds upon this by evaluating the effects of multiple PRP injections in POI patients, allowing us to assess whether repeated treatments lead to improved ovarian function and clinical outcomes. The presentation of these cases typically involved amenorrhea and low serum estrogen levels with elevated gonadotropins, consistent with POI diagnosis. Over the course of treatment, we observed variable responses to repeated PRP injections, with some patients demonstrating sustained follicular development and improved ovarian reserve markers, while others had limited responses.

The two cases in this series exhibited distinct baseline characteristics, including differences in age, ovarian reserve markers (such as AMH and FSH), and duration of amenorrhea, which likely influenced their respective responses to repeated PRP injections and IVF outcomes. Younger patients with relatively higher AMH levels and shorter duration of amenorrhea tended to show more robust follicular development and better clinical responses, consistent with existing evidence that age and ovarian reserve are key predictors of fertility treatment success in POI. Conversely, patients with more advanced age and lower baseline ovarian reserve demonstrated more modest improvements, underscoring the heterogeneity of POI and the need for individualized treatment protocols.[20] Understanding these patient-specific factors is crucial in interpreting clinical outcomes and optimizing PRP therapy for ovarian rejuvenation.

Comparing our findings with the initial Cakiroglu study and other case reports in the literature, which primarily focus on single PRP administrations,[19,21,22] our study suggests that multiple PRP injections may offer a more sustained benefit in follicular activation and ovarian responsiveness. This approach could potentially shift the clinical management of POI by introducing a novel protocol for ongoing ovarian stimulation and improving IVF outcomes for patients with diminished ovarian reserve.

According to standard operational procedure for PRP injection in our fertility clinic, PRP injection is administered when the AMH level falls below 0.5 ng/mL, indicating an inadequate ovarian reserve.[17,19,23,24] AMH levels less than 0.5 ng/mL is predictive of reduced success in management of infertility, therefore the target of AMH >0.5 ng/mL is crucial.[25] The choice to administer numerous PRP injections was made since case 1 had a low AMH level (<0.5 ng/mL) after 1 month of follow-up, and case 2 had a low AMH level (<0.5 ng/mL) after 3 months of follow-up.

Despite the promising observations in this case series, several limitations should be considered. The small sample size of only two patients restricts the generalizability of our findings and limits the ability to draw definitive conclusions about the efficacy of repeated PRP injections. Moreover, as a case series without a control group, it is difficult to exclude the possibility that clinical improvements may be influenced by confounding factors or natural variations in ovarian function. Variability in individual responses to IVF and PRP treatment further complicates interpretation. Larger, controlled studies with longer follow-up are needed to confirm these preliminary findings and to establish standardized treatment protocols.

To best of our knowledge, no prospective or randomized controlled trials have evaluated the impact of numerous platelet-rich plasma injections on primary ovarian insufficiency in women undergoing in vitro fertilization. Furthermore, there was a lack of established standard protocol for PRP injection in patients with POI. From this case series, we can infer that the timing of the second ovarian PRP injection may also influence the result of pregnancy. Additional research with a prospective approach, involving a large population and multiple centers, is necessary.

Conclusion

Platelet-rich plasma (PRP) treatment represents a promising therapeutic approach to enhance ovarian reserve and improve reproductive outcomes in patients with primary ovarian insufficiency (POI), especially those preparing for in vitro fertilization (IVF). Our case series suggests that repeated PRP injections, particularly the timing of the second injection, may influence clinical pregnancy outcomes. However, due to the limited sample size and observational nature of this study, further prospective research with larger cohorts and standardized protocols is essential to validate these findings and clarify the impact of PRP on key clinical endpoints such as pregnancy rates, live birth rates, and ovarian function recovery.

Informed Consent Patient Statement

No formal ethical clearance was required for the publication of this case. The authors confirm that written informed consent for publication of this case report and any accompanying images was obtained from the patient and her spouse. The patient was informed in detail about the case content and agreed to its publication. All personal identifiers have been removed to ensure patient anonymity.

Disclosure

The authors report no conflicts of interest in this work.

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