



Case Report

A new approach of using platelet-rich autologous plasma to increase the ovarian reservoir in a Syrian patient with ovarian insufficiency: A case report

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ABSTRACT

Introduction: The prevalence of Primary ovarian insufficiency (POI) is estimated to be 1–2%, resulting from many causes, including, iatrogenic causes which are becoming more common.

There is no precise treatment to restore fertility in POI patients. However, new treatments -such as ovarian rejuvenation using platelet-rich autologous plasma (PRP)- are being tested and have shown promising results. We report using a new PRP injection protocol to manage a Syrian patient with ovarian insufficiency.

Case presentation: A 35-year-old woman with five years of primary infertility presented with decreased anti-mullerian hormone (AMH) after she underwent a laparoscopy one year ago. Where the AMH dropped from 1.07 to 0.39 ng/mL after it. She underwent an ovarian rejuvenation using PRP. Half mL of PRP was injected into every ovary, 2 mL were injected into the cervix, 7 mL intra-uterus, and 7 mL were injected intramuscularly to the patient's legs. Fifteen days following the operation, the patient's new AMH level was 0.94 ng/mL. The patient was placed on ovarian stimulation, and five days later the ultrasonography showed the development of six follicles in each ovary.

Discussion: Managing POI using ovarian rejuvenation is the best alternative treatment; When the donor eggs programs are not acceptable. The use of PRP in ovarian rejuvenation has been reported to be effective.

Conclusion: The use of PRP was beneficial in restoring fertility in a Syrian patient with ovarian insufficiency. Furthermore, the new PRP injection protocol was successful. However, more studies are needed to confirm this result.

1. Background

Primary ovarian insufficiency (POI), an early occurrence of menopause, is defined as the premature disturbance of menstruation and ovulation before the age of 40 [1]. The prevalence of POI is estimated to be 1–2% [2,3], and most of these cases are idiopathic [4]. Other causes include; Genetic, iatrogenic, and autoimmune causes. Moreover, iatrogenic causes such as surgery are becoming more common due to the increased use of laparoscopy [4]. The high level of follicle-stimulating hormone (FSH) in the blood can confirm the diagnosis [4]. In POI patients, anti-mullerian hormone (AMH) is usually low, reflecting the eggs' reservoir in the ovaries [5].

As far as we know, there is no precise treatment to restore fertility in

POI patients [4]. However, many studies suggested treatments with promising results; Such as ovarian rejuvenation using either stem cell therapy [6] or platelet-rich autologous plasma (PRP) [7]. Nevertheless, the donor eggs programs are still the best choice for POI patients who wish to become pregnant [4].

PRP is a plasma separated from peripheral blood by centrifugation; it contains a high concentration of platelets [8]. When the platelets are activated, they release growth factors that induce proliferation, growth, and differentiation [9]. PRP was used to treat several medical cases such as musculoskeletal injuries and illnesses [10,11]. On the other hand, it was found to have the ability to activate the follicles in POI patients [12].

The injection of PRP directly to the ovaries through laparoscopy was

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reported to be beneficial, as the serum level of AMH significantly increased [13]. However, further studies are still required. Nevertheless, this study reports the first attempt to manage a Syrian patient with ovarian insufficiency using a new PRP injection protocol. This case report has been reported in line with the SCARE Criteria [14].

1.1. Case presentation

A 35-year-old patient presented to our fertility clinic at the University Hospital of Obstetrics and Gynecology in Damascus Syria complaining of primary infertility for five years, with recurrent pregnancy loss, and many previous ovulation induction attempts. She has a regular 28 days menstrual cycle. The patient had a history of well-tolerated systemic lupus erythematosus (SLE), along with well-managed hypothyroidism since January 2021. She was diagnosed with idiopathic tubal adhesions one year ago and underwent laparoscopy as a treatment for the adhesions with no further information about the procedure. Before the laparoscopy, her AMH level was 1.07 ng/mL, with no further relevant information in the patient's medical history.

A whole new assessment was carried out, the physical and gynecological exams were within normal range with a regular menstrual cycle, the Ultrasonography of the ovaries showed no remarkable features, and the Hysterosalpingography showed open fallopian tubes. The lab test showed an AMH of 0.39 ng/mL; other lab tests were within the normal range including the FSH and Estradiol (E2), lupus anticoagulant (LAC), anti-cardiolipin antibodies, anti- β -2-glycoprotein antibodies, and no male factor was found.

After explaining the procedure and taking the patient's consent, she underwent an ovarian rejuvenation using PRP. Twenty cm of blood were extracted from the patient and placed on two stages of centrifugation. The first one was on 1500 revolutions per minute (RPM) for 15 minutes, and the second one was on 2000 RPM for 10 minutes. Following that, the PRP was treated with multiple vitamins and other supplements, and about 20 mL of PRP was collected. The patient underwent a laparoscopy in which 0.5 mL of PRP was injected into each ovary, 2 mL were injected into the cervix, and 7 mL intra-uterus. Furthermore, 7 mL was injected intramuscularly into the patient's thighs. The operation was performed by Dr. Haitham Abbassi, and it went well, with no complications.

After the operation, a close follow-up was done. Fifteen days following the operation, the patient's new AMH level reached 0.94 ng/mL. After that, the patient was placed on ovarian stimulation using 100 Mg of clomiphene citrate. Five days after the stimulation, the Ultrasonography showed the development of six follicles in each ovary (Fig. 1). A planed in vitro fertilization (IVF) was planed. However, we lost contact with the patient.

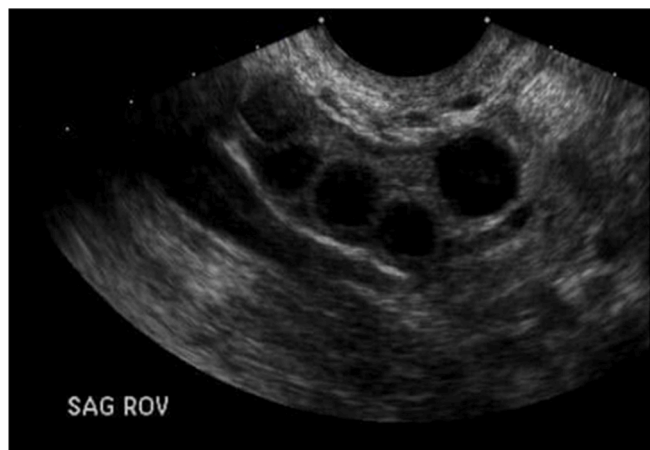


Fig. 1. Transvaginal ultrasound of the Right ovary.

Fig. 1 legend: the ecography shows the development of four follicles ranged between 1.3 and 1.5 cm in diameter.

2. Discussion

POI is the inability of the ovaries to produce enough estrogen or release eggs before the age of 40 [15]. The prevalence of POI is about 1–2% [2,3]. POI occurs due to; Genetic causes like Turner syndrome and Fragile X syndrome, autoimmune diseases, toxins, and iatrogenic causes, while the rest are considered idiopathic [4,16]. The iatrogenic causes are becoming more common due to the increase in the use of laparoscopy and Chemo-radiotherapy, as they reached up to 37% of POI cases in New Zealand [4].

Women with POI usually complain of infertility and other symptoms related to the drop in estrogens level, like irregular or skipped periods, hot flashes, vaginal dryness, and other symptoms [15]. However, women in the early stage of POI may only complain of unexplained infertility or repeated in vitro fertilization (IVF) failures along with normal menses (occult POI) [17]. In our case, the patient's POI was probably iatrogenic induced since the AMH levels dropped dramatically after the procedure. However, a laparoscopy for lysing adhesions won't cause an iatrogenic POI, but since no information about the procedure is available we can not be sure if the POI is iatrogenic or not. The patient complained only of five-year infertility which might be SLE induced. Nevertheless, the rapid drop in AMH levels can not be attributed to the patient's SLE.

The typical diagnosis of POI is usually made after four to six months of amenorrhea in women under the age of 40 years, along with the changes in estradiol and FSH [4]. On the other hand, measuring AMH in diagnosing POI is becoming more common, since it has a high sensitivity to assess the ovarian reservoir. It is usually assessed before and after the surgery, or chemotherapy as a screening procedure for POI [5,17,18]. Our patient underwent a curative laparoscopy, in which she suffered from a significant drop of AMH afterward. Even though she did not meet the diagnosis criteria of POI, she was managed as POI according to her AMH level since it can detect the early stages of POI; In which the FSH and E2 are still within the normal range.

Patients with POI still have a 5–10% chance to conceive spontaneously [19]. On the other hand, there are no guidelines that address the fertility management of POI [4]. Many studies assessed the efficacy of clomiphene, gonadotropins, gonadotropin-releasing hormone (GnRH) agonists and antagonists, glucocorticoids, and menopause hormone therapy [20]. While other studies tested the efficacy of ovarian rejuvenation using stem cell therapy [6,21], and PRP [7]. Nevertheless, the use of donor eggs is still the first-line treatment so far [4,15,22]. In our case, the donor egg was not an option due to religious rejection of such a procedure. After discussing the possible options with the patient, she agreed to go with ovarian rejuvenation with PRP.

PRP is plasma with high platelet concentration, it is created from a patient's autologous blood by centrifugation [23]. It was first known in the 1970s [24], where thrombocytes were found to have a role in cell proliferation [25]. Many centrifugation methods were mentioned in the literature [25], and a similar centrifugation method was used on this patient blood.

The use of PRP injections is effective and safe [7], and many studies pointed at the efficacy of using PRP in ovarian rejuvenation, where it successfully activated the follicles [26,27]. Other studies reported the benefit of directly injecting the ovaries with PRP through laparoscopically assisted technique [27,28]. In our case, we used a similar technique, where we inject the ovaries directly with the PRP through laparoscopy. Moreover, we enhanced the procedure by injecting the PRP into the cervix, intrauterine, and two intramuscular injections. We found this protocol to be effective, where the patient's AMH significantly increased. Six follicles in each ovary were successfully developed, which can not be attributed to the 5–10% chance of spontaneous follicular development in POI patients.

As far as we know this is the first time this protocol is used, so there is no data reported and more research is needed to confirm our results. We think that generalized admission enhanced the localized effects of PRP

and gives better results. However, more studies with proper design are needed to confirm this theory. Furthermore, we were unable to access the effect of this method on the pregnancy outcome, because we lost contact with the patient.

In conclusion, the use of PRP offers a good chance to restore fertility in POI patients. It would be more acceptable treatment than donor eggs programs in countries with religious beliefs. Furthermore, the new PRP injection protocol that we conducted on this patient was effective.

Availability of data and materials

Not applicable.

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Ethical approval

N/A.

Author contribution

RS, RT, DK drafted the manuscript. HA did the procedure and supervised the project. All authors have read and approved the final manuscript.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Guarantor

Professor Haitham Abbassi.

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Declaration of competing interest

The authors declare that they have no competing interests.

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Abbreviations

POI	primary ovarian insufficiency
PRP	platelet-rich autologous plasma
AMH	anti-mullerian hormone
FSH	follicle-stimulating hormone
RPM	revolutions per minute
SLE	Systemic lupus erythematosus
E2	Estradiol
IVF	in vitro fertilization
GnRH	gonadotropin-releasing hormone

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.amsu.2021.103149>.

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