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Case Report

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Successful clinical pregnancy in a poor ovarian responder- A multipronged approach

Abstract

A 38-year-old woman presented with secondary infertility persisting for four years, having previously conceived a child twelve years ago. Her medical history included bilateral ovarian cystectomies due to large dermoids. Investigations revealed a significantly reduced ovarian reserve, indicated by an AMH level of 0.50 ng/mL and FSH of 15. Her partner demonstrated satisfactory semen parameters.

Initial attempts at ovarian stimulation with clomiphene citrate were unsuccessful, prompting a transition to in vitro fertilization (IVF) due to the patient's age and diminished ovarian reserve. However, two IVF cycles with high dose gonadotrophins showed very poor response

Diagnostic hysteroscopy revealed a normal uterine cavity but histological evidence of chronic endometritis, for which the patient underwent a 14-day course of doxycycline.

In a novel approach, the patient opted for ovarian platelet-rich plasma (PRP) injection, aiming for ovarian rejuvenation and improved response. Ultrasound-guided PRP injection was performed, administering two milliliters into each ovary.

Following PRP therapy, a trial of ovulation induction with Letrozole resulted in the development of one dominant follicle, though subsequent ovulation trigger with hCG did not lead to pregnancy.

Laparoscopic evaluation revealed bilateral periovarian adhesions, with the right fallopian tube densely adhered to the pelvic sidewall. Surgically, successfully mobilized adhesion, confirming tubal patency. Both ovaries exhibited reduced size, particularly the left ovary. A second round of PRP injection was administered laparoscopically into each ovary.

One month post-laparoscopy, ovarian stimulation with Letrozole resulted in the development of a single follicle, followed by ovulation trigger with hCG and IUI. Subsequent confirmation of pregnancy via transvaginal ultrasound marked a successful outcome.

The success of this case represents a combination of treatment strategies, including ovarian factor rejuvenation with PRP, selecting an appropriate stimulation regime and IUI, improving uterine receptivity by treating chronic endometritis, and performing tubolysis to confirm bilateral tubal patency followed by timed IUI.

Keywords: pregnancy, ovarian, woman, infertility

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Introduction

A 38-year-old woman presented with secondary infertility persisting for four years, having previously conceived a child twelve years ago. Her medical history included bilateral ovarian cystectomies due to large dermoids. Hormonal investigations revealed a significantly reduced ovarian reserve, indicated by an AMH level of 0.50 ng/mL and FSH of 15. Conversely, her partner demonstrated satisfactory semen parameters.

Initial attempts at ovarian stimulation with clomiphene citrate were unsuccessful, prompting a transition to in vitro fertilization (IVF) due to the patient's age and diminished ovarian reserve. However, the first IVF cycle yielded only one unretrieved egg, while the second cycle, utilizing a short agonist protocol with 450 Units Gonal F, resulted in the retrieval of three eggs, none of which led to successful pregnancy after transfer.

Seeking further expertise, the patient sought consultation at a different fertility clinic. Extensive investigations for recurrent IVF failure, including antiphospholipid screening, yielded negative results. Subsequent diagnostic hysteroscopy revealed a normal uterine cavity but histological evidence of chronic endometritis, for which the patient underwent a 14-day course of doxycycline.

Despite these interventions, a subsequent IVF cycle still demonstrated poor ovarian response, with only two retrieved eggs, both of which failed to develop beyond day three. In a novel approach, the patient opted for ovarian platelet-rich plasma (PRP) injection, aiming for ovarian rejuvenation and improved response in future treatment cycles. Ultrasound-guided PRP injection was performed, administering two milliliters into each ovary.

Following PRP therapy, a trial of ovulation induction with Letrozole resulted in the development of one dominant follicle, though subsequent ovulation trigger with hCG did not lead to pregnancy. In light of the patient's reluctance to pursue further IVF, a diagnostic laparoscopy was recommended to assess tubal status and administer additional PRP injections.

Laparoscopic evaluation revealed bilateral periovarian adhesions, with the right fallopian tube densely adhered to the pelvic sidewall. Surgical intervention successfully mobilized the adhesion, confirming tubal patency. Both ovaries exhibited reduced size, particularly the

left ovary. A second round of PRP injection was administered laparoscopically into each ovary.

One month post-laparoscopy, ovarian stimulation with Letrozole resulted in the development of a single follicle, followed by ovulation trigger with hCG and intrauterine insemination (IUI). Subsequent confirmation of pregnancy via transvaginal ultrasound marked a successful outcome, with rising hCG levels indicative of a viable intrauterine pregnancy.

In summary, this case underscores the complexity of addressing secondary infertility and highlights the role of multidisciplinary interventions, including advanced reproductive techniques and innovative therapies like PRP, in achieving successful outcomes for patients facing fertility challenges.

Discussion

One of the most important factors that limit the success in both natural pregnancy and assisted reproductive technology (ART) is the female age due to reduced ovarian reserve. The Bologna ESHRE consensus defines women as Poor ovarian responder (POR) is defined as presence of at least two of the three characteristics listed below

(1) Maternal age ≥40 years

(2) History of poor ovarian response (≤3 eggs with a conventional stimulation protocol)

(3) Reduced ovarian reserve test (antral follicular count (AFC) <5–7 follicles or AMH <0.5–1.1 ng/ml)

Hence it is obvious that either age should be over 40 years or have undergone one ovarian stimulation cycle for the woman to be considered under this criterion.

Factors affecting ovarian reserve

Various factors can cause a decline in the ovarian reserve apart from the advanced age. Ovarian reserve can be reduced by diseases such as pelvic infections, endometriosis and ovarian surgery. Mechanism of reducing the reserve is multi factorial and can include impaired blood flow, altered intrafollicular hormonal regulatory mechanisms, reduced aromatase and reduced gonadotropin surge-attenuating factor activity.

Poor Ovarian Response (POR)

Prevalence of poor ovarian response to exogenous gonadotropins stimulation is variable ranging from 9% to 24%. This in turn leads to reduced conception and live birth rates ranging from 3% to 14%. One of the studies showed a live birth rate (LBR) of <10% in 821 POR patients who underwent 1,257 ICSI cycles.

POSEIDON criteria

The POSEIDON criteria were developed to address the heterogeneity see among different groups of POR as per the Bologna criteria. POSEIDON criteria uses the female age, ovarian reserve tests, sensitivity of ovary to exogenous gonadotrophins, and the number of eggs retrieved to stratify the patients as low prognosis instead of poor response.

Therapeutic interventions

Basic concepts in various treatment strategies for POR patients include avoiding prolonged pituitary suppression, preventing early luteinizing hormone (LH) surge, and controlled ovarian stimulation (COS) to increase oocyte yield and thereby resulting in embryos with good implantation potential. Inspite of availability of many treatment methods, there is no clear evidence to suggest one is better than the others. Currently practiced techniques include OCP before the stimulation cycle, natural cycle, short agonist and antagonist protocols, high dose FSH, adding LH in early follicular phase, low dose hCG supplements, and the use of adjuvants like androgens, GH, and aspirin.

Antioxidants and supplementation

Newer areas of research include treatment aimed at delaying or partially reversing the diminished ovarian reserve, However as of now there is no evidence based methods available. Various antioxidant dietary supplements containing melatonin, vitamins C and E, dehydroepiandrosterone (DHEA), and coenzyme Q10 are being currently used in pretreatment and treatment cycles to improve the quality and quantity of eggs although there are no supporting clinical trials or meta analysis so far.

Intrauterine Insemination (IUI)

The success rate of intrauterine insemination (IUI) drops considerably with advancing maternal age. Precious time should not be wasted in repeated IUI cycles in women >40 years and not more than one cycle of COS and IUI should be offered. In POR Pregnancy rates are low with all modalities of treatment, with an increased risk of pregnancy loss across all age groups. Hence low threshold to shift to IVF is recommended in POR due to poor pregnancy rates with conventional treatments methods and higher LBR can be achieved by IVF.

Platelet-Rich Plasma (PRP)

Significant advances in tissue engineering have helped regenerate medicine over the past two decades. Platelets play a key role in triggering cell proliferation and tissue differentiation. Platelet-rich plasma (PRP) has platelet concentrations up to seven times higher than circulating serum and is derived from centrifuged whole blood. PRP is being widely used in various fields for tissue and cellular regeneration and hence might play a role in improving the ovarian reserve. Although some studies have shown improved egg quality and quantity with PRP, strong evidence is still lacking and is being practiced empirically in selected situations.

Chronic Endometritis (CE)

Significant number of sub fertile patients with recurrent implantation failure and recurrent pregnancy loss has been shown to have chronic endometritis (CE). Improved clinical pregnancy rates (CPR) and live birth rates (LBR) has been reported recently with broad-spectrum antibiotics. However it is associated with the risk of altering the endometrial flora and developing resistant strains.

Laparoscopic Surgical Correction (LSC)

Laparoscopic surgical correction (LSC) for various conditions like hydrosalpinx, peritubal adhesions, and endometriosis causing tubal infertility has shown to improve CPR with IVF Adhesiolysis for peritubal adhesions, ablation for endometriosis, salpingostomy and fimbrioplasty for treating hydrosalpinx and fimbrial phimosis are the common techniques of LSC. Proximal tubal occlusion can be considered in poor prognosis patients. In mild to moderate periadnexal adhesions after caesarean sections, laparoscopic adhesiolysis should be considered before attempting IVF.[1–13]

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Conclusion

The success of this case represents a combination of treatment strategies, including ovarian factor rejuvenation with PRP, selecting an appropriate stimulation regime and IUI, improving uterine receptivity by treating chronic endometritis, and performing tubolysis to confirm bilateral tubal patency followed by timed IUI.

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Conflicts of interest

The authors report no conflicts of interest.

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