CASE REPORT

Case Report: Case report: Effect of intraovarian platelet-rich plasma therapy on latent female genital tuberculosis patient
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Abstract
Latent female genital tuberculosis (FGTB) has been gaining attention in the world of assisted reproductive technology due to its adverse effect on the female reproductive system, which is becoming a cause of concern in the pathway of fulfilling the dream of children in infertile couples. It has been known to severely affect the ovarian reserve, which is one of the prime causes of infertility in females nowadays. Intraovarian plasma-rich platelet therapy (IOPRP) has been known to improve diminished ovarian reserve (DOR); however, its effect on DOR caused due to latent FGTB is not known. A 34-year-old middle-aged South Asian woman was unable to get pregnant due to being a victim of latent female genital tuberculosis. The patient also had a history of four failed IUI (intra-uterine insemination) cycles prior to their visit to Wardha Test Tube Baby Centre, Sawangi, Maharashtra, in January 2021. The patient had reported having improved ovarian reserve, thereby having positive clinical pregnancy upon the administration of IOPRP at our centre. This case report throws light on the aspect that the use of IOPRP on patient suffering from DOR caused due to latent FGTB may lead to significant positive pregnancy outcomes.

Keywords
Endometrium, Poor ovarian reserve, Dilation and Curettage, Oocyte, Embryo.

This article is included in the Datta Meghe Institute of Higher Education and Research collection.
Introduction
Assisted reproductive techniques have long addressed the ongoing problems in regards to infertility in the world. We have come across various methodologies to strategically handle the root cause of infertility and provide a suitable solution to it. Worldwide, it has been reported that more than 180 million couples are suffering from infertility. Several factors, like thin endometrium, poor ovarian reserve, uterine polyps, etc., are responsible for causing infertility. Out of all the problems, the current trending factor is female genital tuberculosis (FGTB). FGTB is a type of extrapulmonary tuberculosis that has been seeing an increase in trend in young females globally, especially in developing countries. As per the global tuberculosis report, it has been estimated that around 25% of the world’s populace suffers from latent TB, which means they're asymptomatic despite exposure to the TB pathogen Mycobacterium tuberculosis. Endometrial development has reportedly been affected due to the manifestation of TB, which is known to increase harmful cytokines in the decidual layer of the uterus. The descending order of damage caused in the female genital system by FGTB is oviduct (90–100%), hystera (70%), ovaries (30%), cervix (10%) and rarely in the vagina and valvular region (<1%). This is known to cause a decrease in ovarian reserve, which decreases AFC (antral follicular count), followed by low AMH (anti-Mullerian hormone) value, an endometrial lining aberration in the female reproductive region, which leads to infertility.

Instillation of intraovarian platelet-rich plasma therapy (IOPRP) in ovaries has been reported to improve ovarian reserve and enhance AFC and AMH levels, promoting the chances of a successful pregnancy. This case report has been made to highlight the effect of IOPRP on a patient suffering from latent FGTB.

Case presentation
Particulars related to the patient
This case study is based on a middle-aged South Asian couple who selected Wardha Test Tube Baby Centre, Sawangi (M), India, in January 2021 to fulfill their pregnancy dream, hindered by infertility. A 34-year-old middle-aged South Asian woman suffering from secondary infertility for two years out of three years of married life was enrolled for three in vitro fertilisation (IVF) cycles at WTTBC, Wardha. The couple was vividly counselled about the procedure, and duly informed consent was taken from them. The husband was a lecturer by profession, and the wife was a staff nurse. Both parties have no history of smoking, drinking or any addictions.

Medical, family and psychosocial history of the couple
This study gyrates around a woman who was nulligravida. They had no sexual complications in their three years of marital life. She was suffering from secondary infecundity for two years. Semen analysis of the male partner revealed the total sperm count to be 13 million/mL, which is below the lower reference limit as mentioned in WHO 2021 Guidelines. The male partner was diagnosed with mild oligospermia. The normal morphology of sperm was reported to be 10%. The patient was diagnosed with a left ovarian cyst in 2019 and suffered from extrapulmonary tuberculosis, validated by a positive Z.N. Stain report in 2021. Tuberculosis mainly affected her endometrium, causing adhesions along with a milder effect on her ovaries. She also had a history of hypothyroidism for the past year. She was under regular medication of thyroid tablet of 125 μg for the last year. In 2022, between the IVF treatment at WTTBC, Wardha, she also suffered from asymptomatic Covid-19, diagnosed by taking an RT-PCR test, which came to be positive. The couple’s family pedigree was also reported to have hypertension.

The couple also had a history of undergoing IUI (intra-uterine insemination) treatment four times before visiting WTTBC, Wardha. All attempts of IUI failed prior to their IVF treatment at WTTBC, Wardha.

Clinical findings of the patient
AMH (anti-Mullerian hormone) is an essential biomarker to gauge the ovarian reserve present in women. The usual range of serum AMH to predict a healthy ovarian reserve is 2 to 6.8 ng/mL. In our case study, the value of the serum AMH of the patient was 0.4, which is indicative of a meagre ovarian reserve. The patient’s hormonal profile was found to be TSH (thyroid stimulating hormone) 18.09 mIU/L; FSH (follicle stimulating hormone) 4.99 mIU/mL; estrogen 99.319 pg/mL; and LH (luteinizing hormone) 8.97 IU/mL. Upon the use of thyroid supplement tablet of 125 μg for a year, the TSH value was brought down to 3.69 mIU/L. She also had a history of undergoing a diagnostic procedure, dilation and curettage (D&C), with histopathology of the endometrium two years ago to understand the endometrial pathology.

In the first cycle of IVF Treatment, we tried to do a fresh embryo transfer using the self-oocytes of the patient. Gonadotrophin releasing hormone (GnRH) antagonist protocol was followed for the patient. Post this, we administered 10,000 IU of human chorionic gonadotrophin (HCG) injection subcutaneously to the patient, which is responsible for
oocyte maturation. We tried to do transvaginal ovum pick-up 36 hours after the injection application. However, no oocytes were found during the procedure.

The couple was counselled on the following condition, and they were prepared for a second round of IVF treatment. Antral follicular count (AFC) is an effective parameter for analysing ovarian health. The patient reported having 1–2 follicular counts in both ovaries. Lower AFC indicates poor ovarian reserve. We planned to administer IOPRP on both the ovaries for the second round of treatment. We advised the patient to have coenzyme Q10, dehydroepiandrosterone and melatonin combined tablet once a day, and alfacalcidiol 0.5 μg and astaxanthin 8 mg combined pill once a day. From day 2 of the menstrual cycle, we started administering minimal ovarian stimulation protocol using 100 mg of clomiphene citrate till day 6. From day 3, 150–225 units of hMG (human menopausal gonadotrophin) were administered to the patient until one follicle reached 17–18 mm in size. On ovulation day, we performed oocyte retrieval on the patient.

We prepared the IOPRP sample by withdrawing 15 mL of venous blood from the patient in a conical tube. At first, we centrifuged the sample for 10 minutes under 1200 rpm (190 g). The blood is segregated into three layers. The supernatant and the buffy coat (which is believed to have concentrated platelets) were pipetted into a different conical tube and centrifuged for 10 mins under 2000 rpm (535 g). 4 mL of supernatant, which is our PRP sample was collected with the plan of instilling 1–1.5 mL of the sample per ovary. The aspiration procedure was undertaken transvaginally using guided ultrasound by administering mild anaesthesia to the patient. After removing the dominant follicle, we instilled IOPRP in the collapsed follicle for around 45 seconds. We used 1–1.5 mL of PRP for both ovaries. AFC was recorded as 1 in the right ovary and 2 in the left. Upon subsequent follow-up, we performed the oocyte aspiration procedure again, and IOPRP was followed for round 2. Upon the final aspiration procedure, we were able to retrieve 5 MII Oocytes from the patient. We planned to do a fresh embryo transfer with two embryos and freeze the rest of the embryos for frozen embryo transfer. We performed a fresh embryo transfer on the patient. β-HCG report performed after two weeks of the transfer resulted in negative. The couple was counselled and prepared for a frozen embryo transfer.

During the subsequent visit to our centre, we analysed the thickness of the endometrium. The usual range of endometrium is above 7 mm for the transfer of embryos. She was started with oestradiol 2 mg tablet twice daily, vitamin supplements and thyroxine 125 μg as a part of pre-medication.

A globally approved thawing kit was used to thaw the embryo and was stored in a benchtop incubator for around 130 mins for the blastocyst to expand. Once the agenda was achieved, we transferred one embryo of 4AA grade (Figure 1) into the uterus. The patient had no discomfort using the procedure in August 2022.

Figure 1. This shows the embryo that was transferred to the patient.
Follow-up diagnostic evaluation and therapeutic applications

After the successful transfer of the embryo, the patient was discharged with the advice of follow-up. The patient was advised to have ofloxacin and ornidazole combined tablet twice daily, omeprazole 40 mg on an empty stomach daily, vitamin E supplement once a day, arginine tablet once a day, vitamin supplements, oestradiol 2 mg tablet twice a day and progesterone 400 mg once a day. She was also advised to injectables of human chorionic gonadotrophin (HCG), hydroxyprogesterone 500 mg and intralipid injection. After two weeks from the day of embryo transfer, we drew a syringe of blood from the patient and sent it for a β-HCG test at our laboratory centre in ABVRH, Sawangi Wardha. The report came to be positive. The level of β-HCG was reported to be 1050 mIU/mL.

Discussion

Farimani et al. (2021) did a retrospective study on the effect of oocyte variables upon the administration of IOPRP on patients affected by DOR (diminished ovarian reserve) and reportedly found significant positive results. On a similar line, Parikh et al. (2022) conducted a prospective cohort study to analyse the effect on pregnancy outcome on the instillation of IOPRP in young Indian women suffering from infertility due to poor ovarian reserve (POR) and found a significant positive effect. This research formed the basis of our application of IOPRP in our case. The limitation of this case report is that it is performed on a single patient, and the result of this report cannot be generalised in the population. This requires further validation via RCTs (randomised clinical trials) to form baseline treatment in latent FGTB patients seeking IVF treatment.

Due to extrapolating frequency of increase in infertility across the world, it has become a matter of great importance for scientists to research its reasons and fight back with suitable outcomes to continue the human race. There are several reported reasons for infertility found in both males and females, such as low sperm count, sexual dysfunction, aspermia, teratozoospermia etc for men and uterine adhesions, hostile uterine environment, cystic ovary, blocked fallopian tubes etc for females. Latent FGTB has been reported as one of the factors of infertility and caught an upward rising trend for affecting the dreams of several infertile couples desiring for a child. In our case study, the patient was suffering from secondary infertility due to being affected by latent FGTB. Hence, we instigated a venture to study the effect of latent FGTB on the fertility of females and find a possible solution for it. Our patient was in her middle age and was nulligravida; therefore, chances of a normal pregnancy using her own gametes seem to be a feasible option. Latent FGTB is an external form of tuberculosis. It is found to affect the fallopian tube majorly, followed by the uterus, cervix, vagina and slight chances of the valvular region. In our patient, latent FGTB was found to affect her ovarian reserve, thereby causing a diminished ovarian content as well as uterine adhesions presented in the case upon histopathological examination of the endometrium. We discovered several studies which show significantly positive improvement of the ovarian reserve upon the administration of IOPRP in case of poor ovarian response patients. However, there were no studies available on the application of IOPRP in DOR cases which was caused by latent FGTB. It has been reported in some literature that there are several growth factors in PRP that play a vital role in regulating vascular activation and neoangiogenesis by either activating the latent oocytes or stimulating the dormant ovarian stem cells to differentiate and develop into active oocytes. Growth factors (GFs) like VEGF (vascular endothelial growth factor) and bFGF (basic fibroblast growth factor) are important angiogenesis molecules present in PRP, which helps in the vascularisation of granulosa, thereby developing the pioneer corpus luteum into its functionality. Other GFs like BMP-2, BMP-4 and GDF-5 also play an essential role in developing oocyte competency by stimulating the mesenchymal and progenitor stem cells. This is believed to improve the pregnancy rate.

It is also hypothesised by some literature that follicular rupture causes injury to the ovarian epithelium, which activates the stem cells in this region to promote healing. Administration of IOPRP by the needle is thought to be activating a similar effect in the ovaries which improves the AFC in further ovum pick-up.

In our case report, we found that the instillation of IOPRP does improve the AFC in our patient suffering from DOR. We were able to retrieve healthy 5 MII oocytes, which led to a fruitful, positive clinical pregnancy outcome for the patient. This was validated by a positive β-HCG report.

Conclusion

This case report outlines the upbeat sequel of the instillation of IOPRP in the case of a patient suffering from secondary infertility due to the adverse effects of latent female genital tuberculosis on her endometrium and ovaries, thereby resulting in successful clinical pregnancy with the assistance of in vitro fertilisation (IVF) procedure at WTTBC, Wardha, India. This case also throws light on the fact that IOPRP may have a significant positive effect on the utilisation on patients suffering from genital tuberculosis.
Consent
Written informed consent was obtained from the patient and her partner for the publication of their clinical details and clinical images.

Data availability
All data underlying the results are available as part of the article, and no additional source data are required.

References

Comments on this article

Version 1

Reader Comment 22 Jun 2023

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Very informative article.

Competing Interests: No competing interests were disclosed.

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