CASE REPORT

Case Report: The application of sildenafil citrate treatment on cervical tuberculosis patient seeking IVF treatment [version 1; peer review: awaiting peer review]

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Abstract
This case report describes the application of sildenafil citrate treatment in a cervical tuberculosis (TB) patient seeking in vitro fertilization (IVF) treatment. The patient, a 34-year-old female with a history of cervical TB and primary infertility, underwent anti-TB treatment before fertility treatment. Cervical stenosis and a thin endometrium were identified during a transvaginal ultrasound, posing challenges to successful IVF outcomes. Sildenafil citrate, a phosphodiesterase-5 (PDE-5) inhibitor known to improve endometrial blood flow, was administered orally at a dosage of 50 mg, three times daily, starting on the fifth day of the menstrual cycle. The patient exhibited an increase in endometrial thickness, indicating improved receptivity. Clinical pregnancy was achieved. These findings suggest that sildenafil citrate may have the potential as an adjunct therapy to enhance IVF success in cervical TB patients, although further research is needed to validate these results in larger studies.

Keywords
Infertility, Clinical Pregnancy, Embryo, Endometrial Receptivity, Cervical Stenosis

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**Introduction**

Infertility is the inability for a woman to get pregnant after a year or after engaging in unprotected intercourse for an extended period. Primary and secondary infertility are the two different types of infertility. A woman who is unable to get pregnant during routine unrestricted sexual activity is said to have primary fertility. Women who become pregnant once but are unable to become pregnant again or who experience multiple pregnancies are said to have secondary infertility. Worldwide, secondary infertility frequently has an impact on infertility in females. The problem of female infertility affects a woman’s psychological, physical, mental, spiritual, and medical state. Infection in the reproductive system causes secondary sterility in females. The major factors that affect female infertility are age and illnesses linked to infertility leading to secondary infertility. Female sterility is primarily caused by endometrial polyps, ovarian insufficiency, a fallopian obstruction, endometriosis, pelvic adhesion, polycystic ovarian syndrome, and uterine fibroid.

A predictive indicator of assisted reproduction success is endometrial thickness. One of the main reasons why embryo implantation attempts fail is poor endometrial receptivity, which is essential for a healthy pregnancy. In fresh *in vitro* fertilization (IVF) cycles, a thin endometrium is one that is less than 7 mm in diameter on the day of ovulation, the day of the human chorionic gonadotrophin (HCG) injection, or when progesterone is used in frozen-thawed embryo transfer cycles. A thin endometrium is an independent risk factor for pregnancy, whether or not ovarian stimulation is present. Fallopian tube and endometrial defects in the genital tract are caused by genital tuberculosis (TB). The infection causes cervical TB to develop. The cervix can become infected directly or indirectly through lymphatic enlargement. Genital TB signs include abnormal vaginal bleeding, menstrual issues, and abdominal discomfort. This case report focuses on a patient who was suffering from cervical TB and her successful clinical pregnancy.

**Case presentation**

**Patient information**

This case was treated at the Wardha Test Tube Baby Centre, in Wardha. The patient, who was 34 years old at time of treatment, and her partner, who was 36 years old, are the couple featured in this case study. The patient has come for a treatment for infertility because the couple was unable to conceive after two abortions. Out of those, there was an abortion of a three-month fetus. She also had a history of failed IVF treatment. The male partner did not have a habit of smoking, tobacco and alcohol consumption, or any other drugs uses. He did not have any genetic abnormality or any other medical history or treatment history himself or in his family. The male partner’s semen analysis revealed normal sperm parameters, suggesting no male infertility.

After 11 years of marriage, they faced the problem of infertility for ten years. The patient has a significant medical history of cervical TB, which was diagnosed and successfully treated with anti-TB therapy. However, the treatment resulted in scarring and stenosis of the cervix along with effects on the endometrium.

**Clinical findings**

The patient was treated with laparoscopy in 2016 due to abnormality in the pelvis. She was suffering from cervical TB due to an adhesion issue or infection in the lymph. The anti-Mullerian hormone (AMH) value of the patient was 0.62 ng/mL which is a marker for the normal ovarian reserve. The antral follicle count (AFC) was normal. Follicle-stimulating hormone (FSH) value was 5.62 mIU/mL and the luteinizing hormone (LH) value was 2.55 mIU/mL.

In the first ovum pick-up cycle, three oocytes were retrieved, among which two oocytes of the M2 phase and one oocyte of the germinal vesicle stage. Embryos were formed and transferred to the patient. However, no clinical pregnancy was reported as the patient reportedly had a thin endometrium. The couple was referred for a second IVF treatment. We planned for sildenafil citrate treatment for the treatment of thin endometrium in the second cycle of IVF treatment. The patient started receiving sildenafil citrate oral solution at a dose of 50 mg, three times daily, from the fifth day of the menstrual cycle. This time aligns with the endometrium’s proliferative phase to maximize endometrial development and receptivity during the IVF treatment cycle.

The six oocytes of the M2 phase and four oocytes of the M1 phase were retrieved and on day three, the five embryos were formed and frozen. The first frozen embryo was transferred on July 2021. The patient was prescribed sildenafil citrate orally at a dose of 50 mg, to be taken 1 hour before the planned embryo transfer. Embryos were formed and transferred on day 5 as fresh embryo cycle transfer. No complications were observed during treatment.

The IVF procedure followed standard protocols, including controlled ovarian stimulation, oocyte retrieval, and embryo culture. Clinical monitoring following embryo transfer revealed encouraging findings. The embryo transfer procedure was successful, with two high-quality embryos transferred into the patient’s uterus.
Follow up
The doctor suggested medication for her treatment. The medicine prescribed by the doctor was famotidine, dicyclomine hydrochloride and mefenamic acid, ondansetron, diclofenac sodium, estradiol, norethisterone, aspirin, and atorvastatin. After the 14th day, the $\beta$-HCG test was performed at our laboratory in Wardha and was positive. The $\beta$-HCG was 1026 mIU/mL.

Discussion
An uncommon kind of extrapulmonary TB, cervical tuberculosis can harm fertility. In such circumstances, IVF is frequently used to treat infertility, but the success rates could be harmed by weakened endometrial receptivity. In this case report, a patient with cervical TB who was having IVF treatment is discussed, and the possible advantages of utilizing sildenafil citrate as an adjuvant medication.

In this instance, sildenafil citrate was used to increase endometrial receptivity and improve endometrial blood flow. By blocking the decomposition of cyclic guanosine monophosphate (cGMP), which induces vasodilation and increases blood flow, sildenafil citrate, a phosphodiesterase-5 (PDE-5) inhibitor, works effectively. Since 1998, sildenafil citrate has been used as a vasoactive drug for treating male erectile dysfunction. By triggering the cyclic guanosine monophosphate (cGMP) pathway in the penis’ erectile tissue, this selective phosphodiesterase type 5 enzyme inhibitor increases the effects of nitric oxide (NO) on smooth muscle relaxation and vasodilation. Recent studies have shown that constitutive NO synthase and certain mRNAs have similar effects on the rat and human endometrium. The uterine blood flow is improved with sildenafil citrate and causes endometrial growth brought on by oestrogen. Its efficacy has been demonstrated in prior studies to improve endometrial perfusion and outcomes in several fertility-related illnesses.

This case involved a 34-year-old female patient with primary infertility and a history of cervical TB. A transvaginal ultrasound revealed a thin endometrium and cervical stenosis, raising concerns about the efficacy of IVF treatment. Because sildenafil citrate may improve endometrial receptivity, the patient was advised to start taking the medicine.

While receiving treatment, the patient’s endometrial thickness was often measured. It was observed that the endometrial thickness grew, indicating improved endometrial receptivity. This result is consistent with earlier studies that demonstrate sildenafil citrate enhances endometrial blood flow, resulting in improved endometrial growth.

Additionally, the patient became clinically pregnant. These encouraging results imply that sildenafil citrate therapy may have contributed to the success of IVF in this cervical TB patient. Sildenafil citrate may have aided in successful implantation and subsequent clinical pregnancy by increasing endometrial receptivity. The results of this case report are in line with earlier research on the use of sildenafil citrate to enhance IVF outcomes.

It should be stressed that this case report only covers one patient, and that additional research with greater patient populations and controlled trials is required to verify these results. Future studies should also establish the best sildenafil citrate dosage, course, and timing for cervical TB patients seeking IVF therapy.

Conclusions
In conclusion, sildenafil citrate administration as an additional therapy in a cervical TB patient seeking IVF treatment has promise for enhancing therapeutic outcomes. According to this case report, sildenafil citrate improved endometrial receptivity as shown by an increase in endometrial thickness. Inferring that sildenafil citrate may increase the likelihood of successful implantation and pregnancy in cervical TB patients having IVF treatment, the patient was able to get pregnant. Further research is warranted to validate these findings in larger studies and to determine the optimal dosage and duration of sildenafil citrate therapy in this specific patient population. Nonetheless, these preliminary results suggest that sildenafil citrate could be a valuable addition to the management of cervical TB patients seeking IVF treatment, potentially improving their chances of successful outcomes.

Consent
Written informed consent has been obtained from patient and her husband for the publication of this manuscript.
References


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