



Natural Conception Following Lymphocyte Immunotherapy (LIT) in a Patient with Recurrent IVF Failure and Recurrent Pregnancy Loss: A Case Report

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Abstract

Recurrent Implantation Failure (RIF) and Recurrent Pregnancy Loss (RPL) remain significant challenges in assisted reproductive technology. Although the role of Lymphocyte Immunotherapy (LIT) remains controversial, it has been explored in selected patients with suspected immune-mediated reproductive failure. We report a case of a woman with recurrent IVF failure and pregnancy loss who conceived spontaneously following LIT after exhausting multiple fertility treatments.

Keywords: Lymphocyte immunotherapy; Pregnancy; Fertility treatments

Introduction

Recurrent implantation failure and recurrent pregnancy loss are multifactorial conditions involving embryonic, uterine, endocrine, thrombophilic, genetic, and immunological factors [1,2]. The contribution of immune dysregulation to implantation failure has been widely investigated.

Lymphocyte Immunotherapy (LIT) involves the intradermal administration of paternal lymphocytes to induce maternal immune tolerance towards paternal antigens. Although some studies have reported improved live birth rates in carefully selected patients, evidence remains conflicting, and current international guidelines do not recommend its routine use outside selected clinical settings. Nevertheless [3], LIT continues to be offered in certain centers after appropriate counselling.

Case Presentation

A 35-year-old woman presented with primary infertility of seven years' duration. She had previously undergone two Intrauterine Insemination (IUI) cycles, both of which were unsuccessful [4].

Her medical history was significant for hypertension and type 2 diabetes mellitus, both controlled on medication.

Baseline fertility evaluation demonstrated:

- Polycystic Ovary Syndrome (PCOS)
- AMH: 4.82 ng/mL
- AFC: 25
- BMI: 35 kg/m²

Her husband's semen analysis revealed:

- Sperm concentration: 15 million/mL
- Progressive motility: 42%
- Normal morphology: 2%

The couple underwent IVF. Following controlled ovarian stimulation, 12 oocytes were retrieved, of which 11 were metaphase II (MII) oocytes. Despite adequate oocyte maturity, embryo quality was

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suboptimal. Six blastocysts were obtained, including five Grade A and one Grade B embryos.

First Frozen Embryo transfer two Grade A embryos were transferred.

Serum β -hCG was positive; however, the confirmation ultrasound demonstrated only a thickened endometrium without evidence of an intrauterine gestational sac, suggestive of a biochemical pregnancy [5,6].

Subsequent hysteroscopy revealed features of chronic endometritis with multiple micro polyps. The patient received an appropriate course of antibiotics.

Second Frozen Embryo transfer following a two-month interval, a second double embryo transfer using Grade A embryos was performed.

Serum β -hCG measured approximately 1200 mIU/mL. Ultrasound confirmed a single live intrauterine pregnancy. Unfortunately, the patient later presented with vaginal bleeding, and ultrasound demonstrated a missed abortion. Dilatation and curettage were subsequently performed.

PGT-A and Third Embryo Transfer

The remaining two embryos underwent Preimplantation Genetic Testing for Aneuploidy (PGT-A). One embryo was reported as euploid.

Before transfer, hysteroscopy-guided adhesiolysis was performed. Endometrial biopsy was sent for histopathological examination, which was reported as normal.

Transfer of the single euploid embryo resulted in a negative pregnancy test.

Given repeated implantation failure despite transfer of a euploid embryo and correction of identifiable uterine pathology, the patient was counselled regarding immunological treatment options and subsequently underwent Lymphocyte Immunotherapy (LIT).

Outcome and follow-up

Following completion of LIT, the patient conceived spontaneously without further assisted reproductive treatment.

A confirmation ultrasound demonstrated a viable intrauterine pregnancy, currently at 24 weeks of gestation.

Discussion

This case illustrates the complexity of recurrent reproductive failure, where multiple contributing factors including PCOS, obesity, chronic endometritis, miscarriage despite successful implantation, and implantation failure following transfer of a euploid embryo were encountered sequentially [7].

Following treatment of chronic endometritis and optimization of the uterine cavity, implantation failure persisted despite transfer of a chromosomally normal embryo [8-10]. After counselling regarding the uncertain evidence surrounding immunotherapy, LIT was performed. The subsequent spontaneous conception raises the possibility of a beneficial immunomodulatory effect; however, a direct causal relationship cannot be established from a single case.

Spontaneous conception may also represent the natural course following correction of uterine pathology or other unidentified factors.

Learning Points

- Recurrent reproductive failure is multifactorial and requires systematic evaluation of embryonic, uterine, endocrine, genetic, and immunological factors.
- Chronic endometritis should be considered in patients with recurrent implantation failure, as appropriate treatment may improve reproductive outcomes.
- Implantation failure can occur despite transfer of a euploid embryo, highlighting the importance of endometrial and immunological factors.
- Lymphocyte immunotherapy remains an investigational treatment with conflicting evidence and should be offered only after comprehensive counselling and careful patient selection.
- Individual case reports can generate hypotheses but cannot establish treatment efficacy.

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