

Exploring Lymphocyte Immunotherapy as A Treatment For Unexplained Repeated IVF Failure: A Case Study of Immune System Modulation and Positive Clinical Pregnancy

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ABSTRACT

Recurrent implantation failure and repeated in vitro fertilization (IVF) failure remain major challenges in reproductive medicine. Although advances in assisted reproductive technologies have improved pregnancy outcomes, some couples fail to achieve pregnancy despite favorable reproductive parameters and the transfer of good-quality embryos, suggesting a possible role of underlying immunological factors. Lymphocyte Immunotherapy (LIT) has been proposed as an immunomodulatory treatment designed to enhance maternal immune tolerance toward paternal antigens and support successful embryo implantation. We report the case of a 33-year-old woman with a history of infertility and two previous failed IVF cycles despite adequate ovarian reserve, satisfactory reproductive potential, and normal male-factor evaluation. The male partner's semen analysis was within normal reference ranges, and sperm DNA Fragmentation Index (DFI) was normal. No significant medical or surgical comorbidities were identified. In view of unexplained recurrent IVF failure and suspected immune-mediated implantation dysfunction, the patient underwent partner-derived Lymphocyte Immunotherapy prior to a subsequent IVF cycle. Fourteen days after embryo transfer, serum β -human chorionic gonadotropin (β -hCG) was positive at 1801.90 mIU/mL. Follow-up ultrasonography confirmed a viable intrauterine pregnancy at 6 weeks, normal dating at 8 weeks, normal nuchal translucency and nasal bone findings at 11 weeks, and a normal anomaly scan at 22 weeks. The pregnancy progressed uneventfully and resulted in the delivery of a healthy term infant at 39 weeks of gestation. This case highlights the potential role of LIT as an adjunctive treatment strategy in selected patients with unexplained recurrent IVF failure and supports further investigation into immune-based approaches for implantation failure.

INTRODUCTION

Recurrent implantation failure (RIF) is a distressing condition for both patients and clinicians and remains one of the most challenging problems in assisted reproductive technology.^[1] Despite significant improvements in IVF techniques, embryo culture systems, and embryo selection methods, some couples continue to experience repeated implantation failure despite the transfer of good-quality embryos and the absence of identifiable reproductive abnormalities. While uterine, embryonic, endocrine, genetic, and male-factor causes are commonly investigated, immunological mechanisms are increasingly being explored as contributors to implantation failure. Successful implantation and pregnancy maintenance require a carefully regulated maternal immune response that allows tolerance toward the semi-allogenic embryo carrying paternal antigens.^[2] Failure of this immunological adaptation may impair implantation and contribute to recurrent IVF failure and pregnancy loss. Lymphocyte Immunotherapy (LIT), which involves the administration of paternal lymphocytes to the female partner, has been proposed as a method to promote maternal immune tolerance and improve reproductive outcomes. We present a case of unexplained recurrent IVF failure in a young woman who achieved a successful clinical pregnancy and live birth following LIT and a subsequent IVF cycle.

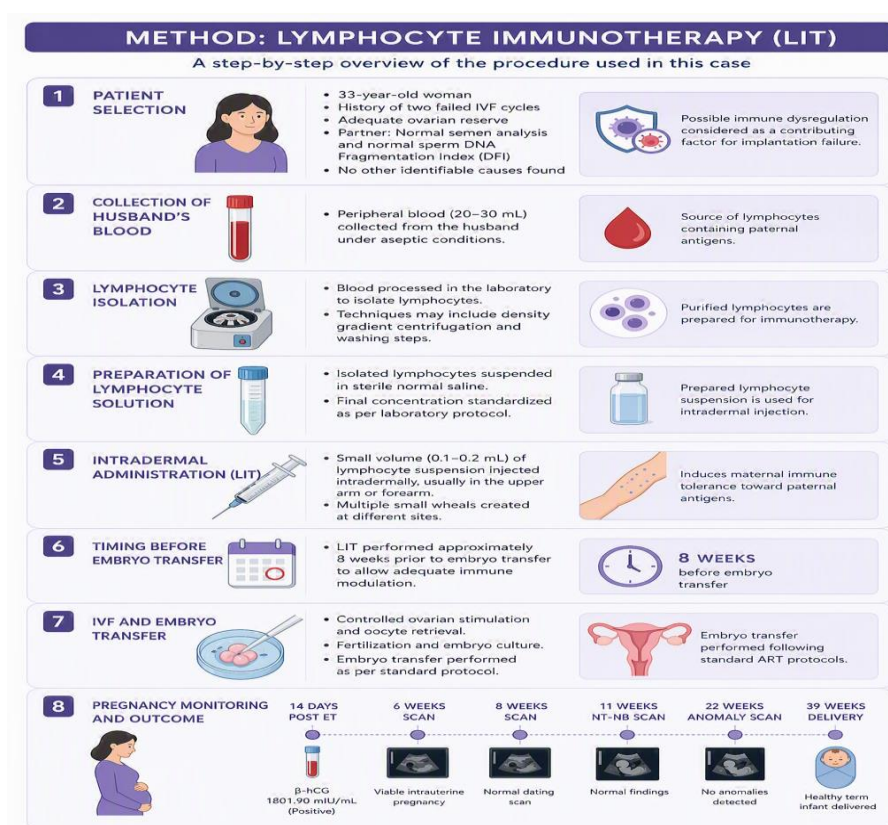
CASE PRESENTATION

A 33-year-old woman presented with a history of primary infertility and recurrent IVF failure. Her chief concern was the inability to achieve pregnancy despite undergoing two previous IVF cycles. Both treatment cycles had failed despite the transfer of good-quality embryos. She had no previous history of spontaneous conception, miscarriage, or live birth. Her medical history was unremarkable, with no known autoimmune disorders, endocrine abnormalities, chronic illnesses, or significant comorbidities. She had no history of previous abdominal or gynecological surgery. There was no significant family history of infertility or pregnancy complications. The emotional impact of repeated treatment failures and uncertainty regarding the cause of infertility were among her major concerns at presentation.

Clinical evaluation revealed no significant abnormalities. Assessment of ovarian reserve demonstrated adequate reproductive potential. Hormonal and fertility parameters were considered satisfactory for conception through assisted reproductive techniques. Evaluation of the male partner showed semen parameters within normal reference ranges according to accepted laboratory standards. Sperm DNA Fragmentation Index (DFI) testing was also normal, indicating good sperm DNA integrity. In view of normal reproductive assessments in both partners and repeated IVF failures despite favourable prognostic factors, immune-mediated implantation dysfunction was considered a possible contributing factor.

The patient initially underwent routine infertility evaluation, which demonstrated satisfactory reproductive parameters in both partners. She subsequently underwent two IVF cycles, both of which failed to result in pregnancy. Following comprehensive reassessment and exclusion of known causes of implantation failure, immune-related factors were suspected. Lymphocyte Immunotherapy was administered prior to initiating another IVF cycle. Embryo transfer was subsequently performed. Fourteen days after embryo transfer, serum β -hCG was positive at 1801.90 mIU/mL. A viability scan at 6 weeks confirmed a normal intrauterine pregnancy. A

dating scan performed at 8 weeks was consistent with gestational age. First-trimester assessment at 11 weeks demonstrated normal nuchal translucency and nasal bone findings. A detailed fetal anomaly scan at 22 weeks showed no abnormalities. The remainder of the pregnancy progressed uneventfully, culminating in the delivery of a healthy term infant at 39 weeks of gestation.



Diagnostic Assessment

The patient underwent standard infertility investigations, including a comprehensive reproductive history, physical examination, ovarian reserve assessment, laboratory investigations, and embryological review of previous IVF cycles. Male partner evaluation included semen analysis and sperm DNA Fragmentation Index testing. No abnormalities were identified that could account for repeated IVF failure. Diagnostic challenges arose because conventional causes of implantation failure, including poor ovarian reserve, embryo-quality issues, male-factor infertility, endocrine dysfunction, and structural reproductive abnormalities, were not evident. Consequently, unexplained recurrent IVF failure with suspected immune-mediated implantation dysfunction was considered the most likely diagnosis. The patient's young age, adequate ovarian reserve, good-quality embryos, and normal sperm parameters represented favorable prognostic characteristics suggesting that successful pregnancy could potentially be achieved if the underlying implantation barrier was addressed.

Therapeutic Intervention

Given the history of repeated IVF failure and the absence of an identifiable cause, the patient underwent partner-derived Lymphocyte Immunotherapy as an immunomodulatory intervention. Peripheral blood lymphocytes were

collected from the male partner, processed according to institutional protocols, and administered intradermally to the patient with the aim of inducing maternal immune tolerance toward paternal antigens. Following completion of LIT, the patient proceeded with a planned IVF cycle and embryo transfer. No significant modifications to the treatment strategy were required during the course of therapy.

Follow-up and Outcomes

The treatment resulted in a successful pregnancy outcome. Fourteen days after embryo transfer, serum β -hCG was measured at 1801.90 mIU/mL, confirming biochemical pregnancy. A transvaginal ultrasound at 6 weeks demonstrated a viable intrauterine gestation with fetal cardiac activity (Figure 1). An 8-week dating scan confirmed normal embryonic development and gestational age. First-trimester screening at 11 weeks, including nuchal translucency and nasal bone assessment, was normal. Detailed anomaly assessment at 22 weeks revealed no fetal structural abnormalities (Figure 2). The remainder of the pregnancy progressed without significant maternal or fetal complications. The patient ultimately delivered a healthy infant at 39 weeks of gestation. Both maternal and neonatal outcomes were favorable.



Figure 1: Scan of 6 weeks pregnancy



Figure 2: Scan mid-trimester anomaly scan (around 20 weeks gestation)

DISCUSSION

This case highlights the possible benefit of Lymphocyte Immunotherapy as an adjunctive treatment approach in selected patients with unexplained recurrent IVF failure. The patient described in this report had experienced two previous unsuccessful IVF cycles despite favorable reproductive characteristics, adequate ovarian reserve, normal sperm DNA integrity, and the absence of identifiable infertility factors.^[2] These findings raised the possibility of an underlying immunological mechanism affecting implantation. Successful embryo implantation requires a finely balanced maternal immune response that promotes tolerance toward paternal antigens while maintaining protective immune functions. Disturbances in this balance have been implicated in recurrent implantation failure and recurrent pregnancy loss. LIT is based on the premise that exposure to paternal lymphocytes may stimulate protective immunological adaptations that facilitate implantation and placental development.^[3]

Following administration of LIT, the patient achieved a successful implantation, a viable clinical pregnancy, and ultimately a healthy live birth. Although it is not possible to establish causality from a single case report, the positive clinical outcome observed in this patient supports the hypothesis that immune modulation may contribute to improved reproductive success in carefully selected cases.^[4] Current evidence regarding LIT remains heterogeneous, and there is ongoing debate regarding its efficacy and optimal clinical application.^[5] Nevertheless, this report adds to the body of literature suggesting that immunological evaluation and targeted immunotherapy may have a role in patients experiencing repeated IVF failure despite otherwise favorable reproductive characteristics. Larger prospective studies and randomized controlled trials are necessary to define patient selection criteria and clarify the true therapeutic value of LIT in reproductive medicine.

PATIENT PERSPECTIVE

After experiencing two unsuccessful IVF cycles, the patient reported significant emotional distress and frustration related to infertility. She expressed concern regarding the absence of a clear explanation for repeated treatment failure despite favorable fertility assessments. The recommendation for Lymphocyte Immunotherapy provided hope for an alternative treatment approach aimed at addressing a potential underlying cause. Following successful conception and the birth of a healthy child, the patient expressed satisfaction with the treatment process and gratitude for the multidisciplinary care received throughout her fertility journey.

INFORMED CONSENT

Written informed consent was obtained from the patient for publication of this case report and all associated clinical information. A copy of the consent form is available upon request.

CONCLUSION

This case highlights the potential role of Lymphocyte Immunotherapy (LIT) as an adjunctive treatment in a patient with unexplained recurrent IVF failure. Following LIT and a subsequent IVF cycle, the patient achieved a successful clinical pregnancy and delivered a healthy term infant at 39 weeks of gestation. Although causality cannot be established from a single case, the favorable outcome suggests that immune modulation may benefit

selected patients with recurrent IVF failure when conventional evaluations are unremarkable. Further large-scale studies are needed to confirm the efficacy and optimal use of LIT in reproductive medicine.

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