Case Report

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Successful pregnancy after lipid emulsion therapy in a woman with recurrent pregnancy loss and recurrent implantation failure: A case report

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ABSTRACT

Rationale: Recurrent pregnancy loss and recurrent implantation failure are frequently linked to immune dysregulation, particularly heightened natural killer (NK) cell activity, cytokine imbalance, and autoantibody presence. Lipid emulsion therapy, originally designed for parenteral nutrition, is increasingly recognized for its immunomodulatory potential in reproductive medicine.

Patient concerns: A 34-year-old woman with five years of infertility, four first-trimester miscarriages, and three failed *in vitro* fertilization (IVF) cycles despite transfer of morphologically optimal embryos presented for evaluation.

Diagnosis: Routine genetic, endocrine, metabolic, thrombophilia, and anatomical investigations were unremarkable. Immunological testing revealed elevated antiphospholipid and anti-thyroid peroxidase (anti-TPO) antibodies, increased NK cell activity, an imbalanced Th1/Th2 cytokine ratio, and raised tumor necrosis factor-alpha (TNF-α), suggesting immune-mediated reproductive dysfunction.

Interventions: The patient underwent IVF with transfer of a single euploid blastocyst following intravenous lipid emulsion therapy (20%, 100 mL), administered before transfer, on transfer day, and biweekly until 12 weeks. Associated therapies included aspirin, enoxaparin, progesterone, levothyroxine, and supplementation.

Outcomes: Serum beta-human chorionic gonadotropin (β-hCG) and ultrasound confirmed pregnancy with subsequent NK cell normalization. The pregnancy was uncomplicated, resulting in spontaneous vaginal delivery of a healthy male infant.

Lessons: Lipid emulsion therapy may improve implantation and pregnancy outcomes in immune-mediated recurrent pregnancy loss and recurrent implantation failure, but larger trials are required to validate efficacy and optimize protocols.

KEYWORDS: Recurrent implantation failure; Recurrent pregnancy loss; Lipid emulsion therapy; Assisted reproductive technology; *In vitro* fertilization

1. Introduction

Recurrent pregnancy loss (RPL) and recurrent implantation failure (RIF) are linked to immune dysregulation, characterized by elevated natural killer (NK) cell activity and diminished Treg function, impairing implantation[1]. Cytokine imbalance delays implantation, while personalized immune therapies improve RIF outcomes. Additionally, genetic and environmental factors also play critical roles in RPL and RIF pathogenesis[2]. Lipid emulsion therapy (LET) reduces lipophilic drug toxicity through a lipid sink mechanism, supporting neurotoxicity management but carrying risks like hypertriglyceridemia and pulmonary toxicity[3].

Letrozole, applied in frozen embryo transfer (FET) cycles, enhances implantation and pregnancy outcomes, particularly in women with polycystic ovary syndrome (PCOS) and endometriosis[4]. LET shows comparable outcomes to artificial cycles in PCOS but yields higher live birth rates in endometriosis, indicating superior effectiveness in this group[5]. Combining LET with human menopausal gonadotropin (hMG) stimulation improves implantation rates while reducing miscarriage and ectopic pregnancy compared to hMG alone[6]. LET does not affect neonatal outcomes but increases gestational diabetes risk, contrasted with

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artificial cycles, while natural cycle FET may yield superior obstetric results[7].

The case study evaluates LET's clinical efficacy and immunomodulatory role in improving implantation and pregnancy outcomes in patients with RPL and RIF.

2. Case presentation

2.1. Patient information

A 34-year-old woman with a five-year history of infertility, four first-trimester miscarriages, and three failed *in vitro* fertilization (IVF) attempts with morphologically optimal embryos was evaluated for RPL and implantation failure. Her medical history was unremarkable except for well-controlled hypothyroidism managed with levothyroxine (75 μg/day). Family history included autoimmune thyroiditis and systemic lupus erythematosus. She maintained a healthy lifestyle, with a body mass index (BMI) of 23.8 kg/m^2, was a non-smoker, abstained from alcohol, and had no significant environmental exposures. Her partner had normal semen parameters. Prior treatments included three ovulation induction cycles with clomiphene citrate, four intrauterine inseminations (IUIs) with controlled ovarian stimulation, and three IVF cycles, all unsuccessful despite adjunctive therapies such as aspirin, progesterone, enoxaparin, and prednisone for suspected immune dysfunction. Pregnancy was not achieved despite these interventions.

2.2. Clinical findings

Clinical and gynaecological examination showed stable vitals, normal genital and cervical findings, an anteverted uterus of normal size and movement, no adnexal abnormalities, and no signs of endocrine dysfunction or pelvic pathology.

2.3. Diagnostic assessment

Investigations showed normal genetic, endocrine, metabolic, thrombophilia, and anatomical findings. The patient carried a heterozygous MTHFR C677T mutation without hyperhomocysteinemia. Immunological testing revealed elevated antiphospholipid antibodies, anti-thyroid peroxidase (anti-TPO) antibodies, increased NK cell activity, an imbalanced Th1/Th2 ratio, and raised tumor necrosis factor-alpha (TNF-α), indicating immune-mediated reproductive dysfunction likely contributing to RPL and RIF. Hysterosalpingography confirmed a normal uterine cavity and tubal patency.

2.4. Therapeutic intervention

A 34-year-old woman with five years of infertility, RPL, RIF, four early miscarriages, and three failed IVF cycles underwent treatment with intravenous LET, combined with aspirin, enoxaparin, progesterone, levothyroxine, and supplementation. Controlled ovarian stimulation yielded seven oocytes, five of good quality, and one euploid 4AA blastocyst was transferred after intracytoplasmic sperm injection (ICSI) and chromosomal screening.

The intravenous LET was given in a doctor-supervised outpatient setting, with persistent monitoring of vital signs prior to, during, and after the infusion. No side effects were observed during or post-infusion. The patient exhibited excellent tolerance to all phases of the therapeutic plan without undergoing any severe side effects.

A Day 3 cleavage-stage embryo was retrieved from the patient with a history of RPL and a history of RIF cycles. The single euploid 4AA blastocyst transferred resulted in the successful birth of a healthy male baby, as shown in Figure 1.

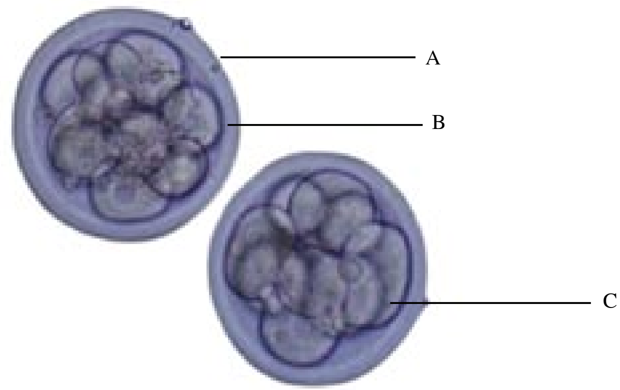

Figure 1. Day 3 embryo from a 34-year-old woman with a history of recurrent pregnancy loss and recurrent implantation failure, where A, B, and C indicate zona pellucida, perivitelline space, and blastomeres, respectively.

2.5. Follow–up and outcomes

The patient underwent IVF with the transfer of a single euploid blastocyst, resulting in a confirmed pregnancy, as indicated by a positive serum beta-human chorionic gonadotropin (β-hCG) level on the ninth day post-transfer and ultrasound at six weeks, showing cardiac activity. First-trimester monitoring demonstrated normalization of NK activity and a favorable cytokine balance. Serial biochemical and ultrasonographic evaluations revealed normal fetal development, with appropriate β-hCG progression, an early gestational sac, yolk sac, embryonic pole, and normal first-trimester screening. A 20-week anatomy scan confirmed growth appropriate for gestational age. The pregnancy remained uncomplicated, resulting in spontaneous vaginal delivery of a healthy male infant at 39 weeks, weighing 3.2 kg, with normal Apgar scores and postnatal assessments.

2.6. Ethical considerations

This case report described a patient who was treated and managed at our IVF centre. As per institutional policy, an individual case report based on routine clinical practice does not require approval from the Institutional Ethics Committee. Informed consent was obtained from the patient for the use of clinical information and its publication.

3. Discussion

LET is hypothesized to suppress elevated NK cell activity in RPL and RIF, producing a favourable uterine environment that may enhance embryo implantation[8]. Third-generation lipid emulsion with omega-3 fatty acids decreases NK cell activity and enhances pregnancy outcomes, demonstrating superior clinical pregnancy rates compared to the controls in a 140-patient trial[9]. Current evidence on LET remains inconsistent, underscoring the need for robust trials to clarify mechanisms, validate efficacy, and establish standardized protocols in RPL and RIF management[8]. Emerging evidence highlights interest in lipid emulsions, yet variability in study designs and outcomes limits definitive conclusions on their efficacy[9]. Few researchers suggest that individual variability in immune responses may limit the effectiveness of LET, emphasizing the need for personalized regimens in RPL and RIF management[8].

Evidence indicates LET may enhance live birth rates in RPL and RIF by downregulating NK cell activity and improving uterine receptivity, offering potential benefit when standard treatments fail[10]. Current evidence is limited by small sample sizes and retrospective designs, underscoring the need for large randomized controlled trials to confirm LET efficacy[9]. Variability in individual responses and lack of standardized dosing protocols delay consistent and effective outcomes with LET therapy[10].

LET demonstrates potential in managing RPL and RIF by modulating NK activity and enhancing implantation. However, inconsistent evidence and variability in dosing protocols require large randomized trials for validation.

In conclusion, LET shows potential as an adjunctive support for managing RPL and RIF in patients with immune-related issues. Clinically, LET may improve outcomes by reducing NK cell activity and restoring cytokine balance, enhancing endometrial receptivity. Despite encouraging results, its routine use remains limited due to inconsistent data and a lack of standard protocols. Well-designed randomized controlled trials are essential to confirm their efficacy and guide clinical decision-making in reproductive immunology.

Conflict of interest statement

There are no conflicts of interest.

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Authors' contributions

Varaganti Pravardhan contributed to the conception or design of the work, drafting of the work, approval of the final version of the manuscript, and agreed on all aspects of the work. Nancy Nair, Varaganti Venkata Sai Suvardhan, Aarya Lele, and Rajasi Sengupta contributed to the literature review, revision of the manuscript for important intellectual content, approval of the final version of the manuscript, and agreed to all aspects of the work.

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References

[1] Raut M, Raut M. Diagnosis of alloimmune factor. In: *Lymphocyte immunization therapy (LIT) in reproductive failures*. Singapore: Springer Nature Singapore; 2022, p. 39-54.

[2] Yousefi M, Aghebati-Maleki L, Chakeri F, Hasani F, Baharaghdam S, Soltani-Zangbar MS, et al. P-385 personalized immunotherapy in RIF patients with different endometrial immune profiles. *Hum Reprod* 2024; **39**(Suppl 1): deae108.740.

[3] Bilvanisi S, Gülen M, Sabak M, Demiryürek Ş, Demiryürek AT. Intravenous lipid emulsion therapy in drug overdose and poisoning: An updated review. *Eur J Med* 2024; **56**(3): 205-212.

[4] Zhang J, Liu H, Wang Y, Mao X, Chen Q, Fan Y, et al. Letrozole use during frozen embryo transfer cycles in women with polycystic ovary syndrome. *Fertil Steril* 2019; **112**(2): 371-377.

[5] Yuan Y, Chang Q, Wen Y, Gao J, Huang S, Xu Y, et al. Letrozole during frozen embryo transfer in women with polycystic ovarian syndrome: A randomized controlled trial. *Obstet Gynecol* 2023; **142**(5): 1087-1095.

[6] Lin J, Wang N, Huang J, Cai R, Fan Y, Kuang Y, et al. Pregnancy and neonatal outcomes of hmg stimulation with or without letrozole in endometrial preparation for frozen–thawed embryo transfer in ovulatory women: A large retrospective cohort study. *Drug Des Devel Ther* 2019; **13**: 3867-3877.

[7] Zaat TR, Kostova EB, Korsen P, Showell MG, Mol F, Van Wely M. Obstetric and neonatal outcomes after natural *versus* artificial cycle frozen embryo transfer and the role of luteal phase support: A systematic review and meta-analysis. *Hum Reprod Update* 2023; **29**(5): 634-654.

[8] Canella PRBC, Barini R, Carvalho PDO, Razolli DS. Lipid emulsion therapy in women with recurrent pregnancy loss and repeated implantation failure: The role of abnormal natural killer cell activity. *J Cell Mol Med* 2021; **25**(5): 2290-2296.

[9] Zhernakova TS, Bespalova ON, Shengelia MO, Kornyushina EA, Pachuliia OV, Postnikova TB. Evaluation of the effectiveness of third-generation lipid emulsion therapy for early pregnancy loss. *J Obstet Womens Dis* 2023; **72**(6): 33-40.

[10]Kumar P, Marron K, Harrity C. Intralipid therapy and adverse reproductive outcome: Is there any evidence? *Reprod Fertil* 2021; **2**(3): 173-186.

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