

Spontaneous Conception After Integrated Traditional Chinese and Western Medicine Treatment for Chronic Endometritis with Recurrent Implantation Failure: A Case Report and Literature Review

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Abstract: Recurrent implantation failure (RIF) is a challenging issue in in vitro fertilization and embryo transfer (IVF-ET). Chronic endometritis (CE) is one of the causes of RIF. For patients with CE and RIF, antibiotic therapy is currently the first-line and most widely used treatment. Nevertheless, it often fails to achieve the desired therapeutic outcomes. This case report presents a woman diagnosed with CE and RIF, who did not achieve pregnancy after four embryo transfers involving a total of seven embryos during IVF-ET treatment. However, after receiving an integrated therapy of Traditional Chinese Medicine (TCM) and antibiotics for CE, the patient achieved a spontaneous conception and subsequently delivered a healthy baby. This case suggests that an integrated approach of TCM and antibiotics may represent a safe and effective therapeutic strategy for patients with CE and RIF, offering a potential alternative to overcome the limitations of conventional antibiotic therapy alone. This finding warrants further investigation.

Keywords: chronic endometritis, recurrent implantation failure, endometrial receptivity, integrative Chinese and Western medicine therapy

Introduction

Embryo implantation is a complex process that involves two critical factors: high-quality embryos and a receptive endometrium. Endometrial receptivity refers to the ability of the endometrium to allow embryo implantation.¹ Recurrent implantation failure (RIF) is defined as the failure to achieve pregnancy despite multiple transfers of high-quality embryos in patients undergoing in vitro fertilization and embryo transfer (IVF-ET). The incidence of RIF among IVF-ET patients is approximately 10%,² leading to significant psychological and financial burdens for infertile couples. The causes of RIF are multifactorial, including maternal, paternal, and embryonic factors. Nowadays, with the continuous improvement of embryo culture systems and the maturation of preimplantation genetic testing, embryonic factors account for only one-third of implantation failures, while endometrial factors contribute to the remaining two-thirds.³

CE is a chronic reproductive tract inflammation characterized by stromal plasma cell infiltration of the endometrium. It is recognized as a significant risk factor for RIF. One study reported the prevalence of CE in infertile women to be between 2.8% and 56.8%, with an incidence of 14% to 67.5% in RIF patients.⁴ In CE, dysbiosis of the endometrial microbiota disrupts the normal intrauterine microenvironment, leading to alterations in local endometrial immune status. This disturbance triggers abnormal immune responses and dysregulated expression of immune factors, ultimately contributing to embryo implantation failure.⁵ Additionally, aberrant angiogenesis represents another significant pathological alteration associated with CE. Endometrial nutrition and oxygen supply depend on adequate vascularization,⁶ and



appropriate angiogenesis is considered a crucial marker of endometrial receptivity. Consequently, impaired angiogenesis is regarded as a key factor in the development of RIF.⁷ Antibiotic therapy is a commonly used treatment for CE. While it can partially eliminate local inflammation and improve the cure rate of CE, it may not significantly improve pregnancy outcomes in patients with CE and RIF.⁸ Further research is needed to identify safer and more effective pharmacological treatment options.

Here, we report a case of a patient with RIF due to CE, who successfully achieved a spontaneous conception and successfully delivered a healthy full-term male infant after treatment with oral Traditional Chinese Medicine (TCM) and antibiotics. The patient initially sought IVF-ET treatment for infertility, undergoing ovarian stimulation and oocyte retrieval twice, with 4 embryo transfers, totaling 7 embryos, none of which resulted in pregnancy. After being diagnosed with CE, she received a combined treatment with TCM and antibiotics, resulting in a subsequent spontaneous conception. To our knowledge, it is rare for patients with recurrent implantation failure in IVF-ET treatment to achieve spontaneous conception. The entire treatment process of the patient is illustrated in Figure 1.

Case Presentation

The patient is a 34-year-old woman who married in 2019. She has regular menstrual cycles and normal sexual activity. In 2019, she underwent laparoscopic right salpingotomy with embryo removal for a right ectopic pregnancy. In 2020, a hysterosalpingogram indicated that both fallopian tubes were patent but with limited flow. Later that year, she underwent a combined hysteroscopic and laparoscopic pelvic adhesion removal and bilateral fallopian tube cannulation. During the surgery, the right fallopian tube was found to be twisted and adhered to the right ovary, while the left fallopian tube appeared normal. The tubal patency test showed that the left fallopian tube was patent, while the right fallopian tube was obstructed.

In April 2021, the patient's anti-Müllerian hormone (AMH) level was measured at 2.55 ng/mL, and she began undergoing ovulation induction treatment. Four cycles of follicular monitoring were performed, with dominant follicle growth and ovulation observed in each cycle. Despite guidance for timed intercourse, pregnancy was not achieved. Subsequently, due to the impact of the COVID-19 pandemic, the patient attempted conception independently for two years without success. In July 2024, the patient's AMH level was rechecked at 1.21 ng/mL. She sought consultation at the Reproductive Medicine Center of Zhongda Hospital, Southeast University, requesting IVF-ET treatment.

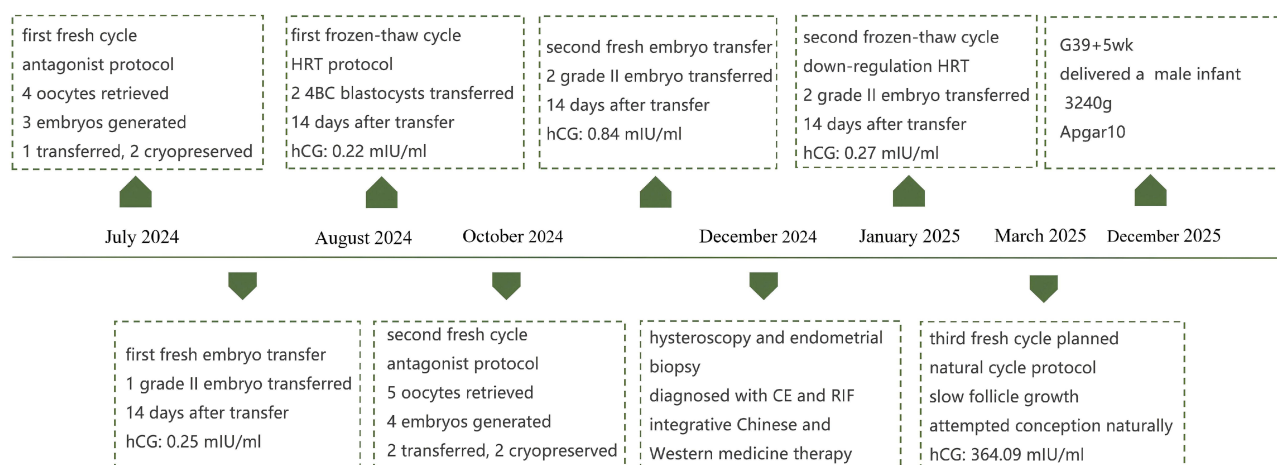


Figure 1 Timeline of the patient's entire treatment process. The patient has undergone assisted reproductive technology treatment since July 2024. The treatment course included 2 ovarian stimulation cycles with oocyte retrieval, resulting in 4 embryo transfers of 7 embryos in total, none of which led to a successful pregnancy. In December 2024, she was diagnosed with CE and RIF. Following a combined treatment of TCM and antibiotics, she achieved a spontaneous conception and successfully delivered a full-term, healthy male infant. Both the mother and child are in good health.

Abbreviations: hCG, human chorionic gonadotropin; HRT, hormone replacement therapy; CE, chronic endometritis; RIF, recurrent implantation failure; TCM, Traditional Chinese medicine.

Before initiating controlled ovarian stimulation (COS), the patient and her partner underwent a series of evaluations to assess their overall health and fertility. No other systemic diseases were identified in either partner. The basic information of the couple, along with the fertility-related test results, are presented in Table 1.

In July 2024, for the first fresh cycle, an antagonist protocol was selected for COS. On the third day of the patient's menstrual cycle, gonadotropin (Gn) was used to initiate ovarian stimulation, with daily subcutaneous injections of recombinant human follicle-stimulating hormone 225IU (r-hFSH, Gonal-f, Merck Serono GmbH, Germany). Regular vaginal ultrasounds were conducted to assess follicular growth and adjust Gn dosage accordingly. On the 6th day of Gn administration, ganirelix 0.25mg (Orgalutran, Organon, Netherlands) was added. After 9 days of Gn treatment, human chorionic gonadotropin 10,000IU (hCG, Qingdao Guanlong Biopharmaceutical Co., Ltd., China) was injected as a trigger, and oocyte retrieval took place 36 hours later, yielding 4 oocytes. Three embryos were generated, with one grade II cleavage-stage embryo transferred on day 3 post-retrieval, and the remaining two blastocysts (4BC) were cryopreserved. The blood test conducted 14 days post-transfer indicated a negative pregnancy.

In August 2024, during the first frozen-thaw cycle, a hormone replacement therapy (HRT) protocol was used. Estradiol (Femoston red tablets, Abbott Biologicals B.V., USA) were taken starting on day 2 of the patient's menstrual cycle to prepare the endometrium. When the endometrial thickness reached 8.2mm, a combination of vaginal progesterone gel 90mg (Crinone, Merck KGaA, Germany) and Femoston yellow tablets was administered for luteal phase support. After 6 days, the embryos were thawed and two 4BC blastocysts were transferred, but the pregnancy was not achieved.

In October 2024, for the second fresh cycle, an antagonist protocol was again chosen for COS. Ovarian stimulation started on day 2 of the patient's menstrual cycle with daily subcutaneous injections of r-hFSH 225IU, recombinant human luteinizing hormone 75IU (r-hLH, Luveris, Merck Serono GmbH, Germany), and recombinant human growth hormone 4IU (rhGH, Jintropin, Changchun Jinsai Pharmaceutical Co., Ltd., China). On day 5 of Gn treatment, ganirelix 0.25mg was added. After 10 days of Gn therapy, hCG 10,000U and triptorelin 0.1mg (Decapeptyl, Ferring Pharmaceuticals Co., Ltd., Switzerland) were injected as trigger. Oocyte retrieval was performed 36 hours later, yielding 5 oocytes. A total of 4 cleavage-stage embryos were formed, and on day 3 post-retrieval, one grade I and one grade II cleavage-stage embryo were transferred, while the remaining two grade II cleavage-stage embryos were cryopreserved. The blood test result 14 days after the transfer still indicated no pregnancy.

In December 2024, following three failed embryo transfers, the patient underwent hysteroscopy and endometrial biopsy with pathological and immunohistochemical analysis, which revealed CE, with positive results for both CD38 and CD138. The patient typically presents with symptoms such as easy fatigue, generalized weakness, abdominal distension

Table 1 Characteristics and the Fertility-Related Test Results of the Couple

Female	Age (years)	34
	BMI (kg/m ²)	21.80
	Duration of infertility (years)	3
	AMH (ng/mL)	1.21
	bFSH (mIU/mL)	5.55
	AFC	8+3
	CA125 (U/mL)	8.03
Male	Age (years)	35
	BMI (kg/m ²)	25.39
	Duration of infertility (years)	3
	Semen volume (mL)	2.9
	Sperm count (/mL)	37.7×10 ⁶
	PR (%)	51.4
	Normal sperm morphology (%)	4.5

Abbreviations: BMI, body mass index; AMH, anti-Müllerian hormone; bFSH, basal follicle-stimulating hormone; AFC, antral follicle count; PR, progressive motile spermatozoa.

Table 2 Treatment Details During Assisted Reproductive Technology Cycles

Treatment Month	Cycle Type	Treatment Protocol	Transferred Embryo(s)	Treatment Outcome
July 2024	Fresh cycle	Antagonist protocol	1*Grade II	2*4BC, Cryo, Non-pregnant
August 2024	Frozen-thaw cycle	HRT	2*4BC	Non-pregnant
October 2024	Fresh cycle	Antagonist protocol	1*Gradel+1*Grade II	2*Grade II, Cryo, Non-pregnant
January 2025	Frozen-thaw cycle	Down-regulation HRT	2*Grade II	Non-pregnant

Abbreviations: Cryo, cryopreserved; HRT, hormone replacement therapy.

after meals or in the afternoon, and occasional loose stools. Physical examination reveals a pale tongue with a thin white coating and a fine, weak pulse. Based on TCM diagnostics, the condition was identified as spleen deficiency with dampness obstruction. The patient was prescribed oral TCM for strengthening the spleen and eliminating dampness, in combination with doxycycline hyclate 100mg (Jiangsu Lianhuan Pharmaceutical Co., Ltd., China), twice daily, for a duration of 2 weeks.

In January 2025, the second frozen-thaw cycle was conducted using a down-regulation HRT approach. On day 4 of the patient's menstrual cycle, a subcutaneous injection of leuporelin acetate 3.75mg (Boenleu, Beijing Bontac Pharmaceutical Co., Ltd., China) was administered. After 28 days, estradiol were taken to prepare the endometrium. When the endometrial thickness reached 8mm, vaginal progesterone gel, estradiol and dydrogesterone (Femoston yellow tablets, Abbott Biologicals B.V., USA) were given to support luteal phase. Four days later, two grade II cleavage-stage embryos were thawed and transferred, but the pregnancy was negative. The treatment details during the assisted reproductive technology cycles are presented in Table 2.

In March 2025, a natural cycle protocol was planned for another oocyte retrieval attempt. Ovulation monitoring began on day 3 of the menstrual cycle, but due to slow follicular growth and a decreasing trend in estrogen levels, the retrieval was canceled. An injection of hCG 10,000IU and triptorelin 0.1mg were administered to induce ovulation. The patient attempted conception naturally, and after ovulation, oral dydrogesterone 30mg/day (Duphaston, Abbott Biologicals B.V., the Netherlands) was prescribed for luteal phase support. Fourteen days later, the patient's serum hCG level was 364.09 mIU/mL, which rose to 1162.22 mIU/mL upon re-examination two days later. Follow-up ultrasound examination confirmed a single intrauterine pregnancy. At 12 weeks of gestation, transvaginal ultrasound confirmed a continuing intrauterine pregnancy, after which luteal support medication was discontinued. The patient underwent regular prenatal check-ups in the obstetrics clinic. On December 21, 2025, at 39 weeks and 5 days of gestation, she successfully delivered a healthy male infant weighing 3240 g, with an Apgar score of 10.

Discussion

Although IVF-ET technology has advanced rapidly in recent years, bringing hope to numerous couples struggling with infertility, RIF continues to be a major challenge and pressing issue in the field of reproductive medicine. So far, a standardized definition of RIF has not been established; however, two diagnostic criteria are widely applied and acknowledged in clinical practice. The first defines RIF as failure to achieve pregnancy after two or more embryo transfer attempts, involving at least two high-grade blastocysts or four high-grade cleavage-stage embryos.⁹ The second criterion describes RIF as the inability to achieve a clinical pregnancy in women younger than 40 years after transferring at least three high-quality embryos across three fresh or frozen cycles.¹⁰ The etiology of RIF is complex, and any factor that affects embryo quality or endometrial receptivity may serve as a potential cause. As one of the conditions that disrupts the intrauterine environment, CE is a common and significant cause of RIF that should not be overlooked.

Contemporary understanding holds that the endometrium harbors hundreds of microbial communities that dynamically modulate its microecological balance, thereby maintaining the microenvironment essential for maternal–fetal interface formation. CE is a condition characterized by localized active infection of the endometrium, which disrupts the balance between the endometrial microbial environment and the immune system. Microbial infections are regarded as the main etiological factor of CE, and the commonly acknowledged pathogens include *Streptococcus species*, *Escherichia coli*,

Staphylococcus, *Enterococcus faecalis*, and *Mycoplasma*. In recent years, CE has garnered increasing attention in the field of assisted reproduction due to its negative impact on embryo implantation. Numerous studies have demonstrated that CE adversely affects embryo implantation and is closely associated with adverse pregnancy outcomes.^{11,12}

CE can reduce endometrial receptivity through multiple mechanisms, thereby impairing embryo implantation. Firstly, microbial infection in CE patients leads to dysbiosis of the endometrial microbiota, primarily characterized by altered abundance of *Lactobacillus*,¹³ which is the main factor affecting embryo implantation. Secondly, microbial infection within the uterine cavity of CE patients leads to immune microenvironmental alteration,^{14,15} where dysregulated expression of immune and inflammatory cytokines diminishes endometrial receptivity. In addition, CE interferes with endometrial decidualization by modulating the expression of estrogen and progesterone receptors, thus preventing successful embryo implantation.¹⁶

The majority of patients with CE present with no typical clinical symptoms or only mild, nonspecific manifestations such as increased vaginal discharge or pelvic discomfort. These subtle manifestations are frequently overlooked in clinical practice, constituting a major diagnostic challenge. The main pathological features of CE include endometrial mucosal edema, separation of epithelial cells and stroma, increased stromal cell density, and infiltration of plasma cells in the stroma,¹⁷ among which the presence of plasma cells in the stroma is the most specific and sensitive indicator. The diagnostic methods for CE include hysteroscopic examination, histopathological evaluation, pathogenic microbial culture, and next-generation sequencing (NGS) techniques. Although characteristic hysteroscopic findings of CE, such as punctate hemorrhage or the “strawberry sign” are relatively intuitive, a study by Song et al¹⁸ reported that the overall diagnostic accuracy of hysteroscopy for CE is only 67%. Therefore, hysteroscopy alone cannot be used as a definitive diagnostic method for CE. The current preferred diagnostic approach is a combination of hysteroscopic examination, endometrial histopathological assessment, and immunohistochemical staining for CD138.¹⁵ However, there is still no consensus regarding the required density of plasma cells in the endometrial stroma (ie, the number of plasma cells within a given area). In practice, the presence of more than five plasma cells per high-power field is generally used as the diagnostic criterion.

At present, oral antibiotics are the first-line and most widely used treatment option in clinical practice,^{10,19} which can improve endometrial receptivity and thereby increase the success rate of subsequent transfer cycles. In a 2017 prospective study, Kitaya et al²⁰ evaluated pregnancy outcomes in 118 women with RIF and concomitant CE following antibiotic treatment. They found that the live birth rate in the first embryo transfer cycle (32.8%) and the cumulative live birth rate over three cycles (38.8%) in the CE-cured group were both higher than those in the non-CE group (22.1%, $P = 0.031$; 27.9%, $P = 0.037$). Management of CE has likewise been shown to enhance in vitro fertilization (IVF) outcomes among patients with RIF.²¹ However, due to the limitations of endometrial microbial pathogen culture, the treatment of CE remains largely empirical. There is still no standardized guideline regarding the selection, duration, dosage, or administration of antibiotics, and prolonged or high-dose regimens may lead to antibiotic resistance and compromise therapeutic efficacy. Evidence indicates that despite undergoing three courses of antibiotic therapy, 18.75% of patients continue to exhibit persistent CE.²² Additionally, a separate study demonstrated that even following antibiotic therapy, the embryo implantation rate in subsequent transfer cycles of RIF patients with CE (11.5%) was still markedly lower than that of RIF patients without CE (32.7%).²³ Thus, in cases with widespread plasma cell infiltration or antibiotic resistance, antibiotic therapy alone may play a limited role in managing CE. In recent years, multiple strategies including combined antibiotic therapy, oral antibiotics with intrauterine infusion, and antibiotics combined with corticosteroids have been applied for the treatment of CE with concurrent RIF, yet their therapeutic effectiveness still requires further investigation. One study demonstrated that a new treatment strategy combining oral antibiotics (doxycycline and metronidazole) with intrauterine infusion (gentamicin and dexamethasone) could enhance pregnancy outcomes in CE patients with RIF, compared with oral antibiotic therapy alone.²⁴ Nevertheless, the study by Zou et al²⁵ revealed that oral co-administration of prednisone acetate and doxycycline might be an effective treatment option for patients with RIF accompanied by CE and could enhance reproductive outcomes, although it did not improve the CE cure rate compared with doxycycline monotherapy. Moreover, a subset of CE cases may be linked to non-infectious etiologies. In these patients, antibiotics show no therapeutic effect, and effective alternative treatment strategies are still unavailable.

In recent years, TCM has demonstrated considerable therapeutic value and remarkable clinical effectiveness in managing CE associated with RIF.²⁶ In TCM, CE is classified as a type of “dai xia disorder” (abnormal vaginal discharge).

It is believed that weakness of spleen qi results in impaired transformation and transportation of fluids, causing dampness to flow downward to the lower burner. As noted in Fu Qingzhu's Gynecology: "All vaginal discharge syndromes originate from dampness". Zhu Danxi remarked, "When damp-heat invades the blood, prolonged exposure leads to turbidity and stagnation". The primary pathogenesis of CE involves spleen deficiency, qi stagnation, and damp-heat with blood stasis. Hence, therapeutic principles emphasize tonifying qi, strengthening the spleen, nourishing and invigorating the blood, and resolving dampness and swelling. A study reported that the treatment principle of invigorating qi, activating blood circulation, clearing heat, and resolving dampness was effective in managing female infertility induced by CE.²⁷ Jing Wenjun et al²⁸ demonstrated that the modified Danggui Shaoyao San could alleviate endometrial inflammation in CE patients with RIF by improving the development of endometrial pinopodes and downregulating the expression of inflammation-related factors, thereby enhancing endometrial receptivity.

This patient underwent four embryo transfer procedures, with a total of seven embryos transferred (including five high-quality embryos), yet none resulted in successful pregnancy. Throughout the entire IVF-ET treatment process, except for the diagnosis of CE confirmed by hysteroscopy combined with endometrial pathology and immunohistochemistry, no additional abnormalities were found that might have negatively influenced embryo implantation. Following treatment with a spleen-strengthening and dampness-resolving prescription in combination with doxycycline, the patient conceived naturally, which was an unanticipated yet encouraging result for individuals suffering from CE associated with RIF. The spleen-strengthening and dampness-resolving formula consists of 12 herbs, including raw *Astragalus membranaceus* (Huangqi), stir-fried *Atractylodes macrocephala* (Baizhu), *Saposhnikovia divaricata* (Fangfeng), *Dioscorea opposita* (Huai Shanyao), raw *Coix lacryma-jobi* (Yiyiren), *Cinnamomum cassia* twig (Guizhi), *Pseudostellaria heterophylla* (Taizishen), *Poria cocos* (Fuling), honey-fried *Glycyrrhiza uralensis* (Zhigancao), *Angelica sinensis* (Danggui), *Spatholobus suberectus* (Jixueteng), and processed *Cyperus rotundus* (Zhixiangfu). It is a prescription formulated by Professor Jin Baofang based on his clinical experience in treating chronic endometritis. Huangqi functions as the chief herb, invigorating qi, relieving stagnation, and promoting diuresis to alleviate edema. Baizhu fortifies the spleen and promotes fluid metabolism; Taizishen and Shanyao replenish qi and support spleen function; Fuling and Yiyiren reinforce the spleen, leach out dampness, induce urination, and expel pus. Acting synergistically, these herbs aid the principal herb in strengthening qi and spleen function, resolving dampness, and alleviating edema, thus serving as the minister herbs. Guizhi, Xiangfu, Danggui, and Jixueteng collectively warm yang, unblock the meridians, regulate qi, and invigorate blood. Fangfeng dispels wind and overcomes dampness, reinforcing the damp-resolving effects of the minister herbs; these ingredients together constitute the assistant herbs in the formula. Zhigancao coordinates and harmonizes the other components of the prescription, functioning as the messenger herb. The prescription as a whole functions to fortify the spleen, tonify qi, activate blood circulation, dredge meridians, resolve dampness, and relieve swelling. By employing the gentle "sweet and bland" method to remove dampness and emphasizing spleen-strengthening and qi-invigorating herbs, it achieves dampness elimination without injuring yin. In addition, the combined use of strategies that promote blood flow, regulate qi, and dispel wind enhances inflammation resolution through multiple mechanisms, fundamentally treating chronic endometritis. Despite the failure to achieve pregnancy in the first transfer cycle after combined Chinese and Western medical therapy, this outcome does not invalidate the effectiveness of the pharmacological treatment. In reality, no large-sample systematic studies have yet determined the ideal time after CE treatment for achieving the most receptive endometrial condition to maximize implantation success, and performing embryo transfer immediately after treatment does not guarantee satisfactory pregnancy results. According to the study by Xie et al²⁹ antibiotic therapy in CE associated RIF patients led to a marked improvement in the one-year clinical pregnancy rate compared with untreated RIF patients without CE, with the most pronounced effect observed after the fourth month post-treatment. Thus, we are convinced that the combined application of traditional Chinese and Western medicine in treating CE enhanced the patient's endometrial receptivity, which ultimately allowed for spontaneous conception.

Admittedly, this case report has certain limitations. In view of the potential adverse effects of repeated hysteroscopy and endometrial scraping on the endometrium, we did not re-examine the patient's post-treatment endometrial pathology or immunohistochemical findings. This single case does not reflect the full spectrum of similar patients. More extensive clinical data are necessary to confirm the treatment's effectiveness, and additional research is warranted to clarify the mechanisms responsible for its efficacy.

Conclusion

In conclusion, the combination of TCM with antibiotic therapy may be beneficial in the management of CE. For patients with CE accompanied by RIF, an integrative approach could represent a promising therapeutic strategy to support pregnancy achievement. Nevertheless, more research is required to clarify the impact of integrative therapy on CE and its potential benefits for CE associated RIF.

Abbreviations

AMH, anti-Müllerian hormone; CE, chronic endometritis; COS, controlled ovarian stimulation; Gn, gonadotropin; hCG, human chorionic gonadotropin; HRT, hormone replacement therapy; IVF-ET, in vitro fertilization and embryo transfer; NGS, next-generation sequencing; r-hFSH, recombinant human follicle-stimulating; rhGH, recombinant human growth hormone; r-hLH, recombinant human luteinizing hormone; RIF, recurrent implantation failure; TCM, traditional Chinese medicine.

Data Sharing Statement

Please contact the first author or corresponding author for data requests.

Ethics Approval and Consent to Participate

This case report was reviewed and approved by the Ethics Committee of Zhongda Hospital Affiliated to Southeast University, 2024ZDSYLL091-P01. Written informed consent was obtained from the participant.

Consent for Publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

All authors declare no competing interests in this work.

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