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Overcoming infertility in congenital hypogonatotrpic hypogonadism and SLE: A Multidisciplinary ART success

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Abstract
This case report details the successful conception and delivery of a patient with congenital Hypogonadotropic Hypogonadism (CHH) undergoing Assisted Reproductive Technology (ART). The patient had a history of autoimmune conditions, poor ovarian reserve, and a prior failed ART attempt. A comprehensive approach involving ovarian stimulation, endometrial priming, and immune modulation led to a successful pregnancy. This case highlights the importance of personalized ART protocols in managing complex infertility cases.

Keywords: Congenital hypogonadotropic hypogonadism, assisted reproductive technology, ovarian stimulation

Introduction
Hypogonadotropic hypogonadism (HH) is characterized by gonadal hypofunction secondary to deficient gonadotropin drive. In congenital (CHH), impaired hypothalamic secretion or pituitary response to GnRH leads to low Follicle-Stimulating Hormone (FSH), Luteinizing Hormone (LH), and estrogen levels, resulting in anovulation and infertility [1].
CHH may be associated with anosmia (Kallmann syndrome) or occur in its normosmic form. Affected women often present with primary amenorrhea, absent pubertal development, and a hypoplastic uterus. Restoration of fertility requires exogenous gonadotropins or pulsatile GnRH therapy; [2] however, these patients pose additional challenges due to suboptimal endometrial receptivity and reduced uterine volume.
This report describes successful conception in a woman with CHH and systemic lupus erythematosus (SLE) through an individualized ART approach that integrated hormonal, endometrial, and autoimmune management.

Case Description
A 34-year-old woman presented with two years of primary infertility. She was diagnosed with congenital hypogonadotropic hypogonadism at age 13 and had her menses induced after evaluation for primary amenorrhea.
She also had systemic lupus erythematosus (SLE), diagnosed in 2015, and was on maintenance therapy with hydroxychloroquine 200 mg under rheumatologic supervision. Her baseline hormone profile revealed: FSH 1.6 IU/L, LH 1.3 IU/L, and estradiol 13 pg/mL. Thyroid function and prolactin were within normal limits.
Pelvic ultrasound revealed a hypoplastic uterus (3.8 × 3.2 × 2.9 cm) and bilateral small ovaries with 3-4 antral follicles each. Her husband's semen analysis was normal. A prior IVF cycle with a single embryo transfer had been unsuccessful.
Given the complex endocrine and autoimmune background, a comprehensive individualized ART plan was implemented. Pre-treatment included antioxidant supplementation including Coenzyme Q10 100 mg and Glutathione 500 mg and low-dose aspirin (100 mg daily) to improve uterine perfusion and reduce oxidative stress.
Controlled ovarian stimulation was initiated using Antagonist protocol with human menopausal gonadotropin (HMG) 375IU. Dose monitoring was guided by serial ultrasound and estradiol monitoring. A total of 20 oocytes were retrieved, 16 were mature, and 15 fertilized. Three blastocysts were developed and cryopreserved.

Sequential estrogen-progesterone therapy was administered for four months to enhance uterine development. *Estradiol valerate* was given sublingually and titrated gradually over cycles to mimic physiological estrogen rise. Progesterone was introduced from day 18-28 of each cycle for withdrawal bleeding.

During the transfer cycle, the patient received transdermal estradiol patches (100 µg every three days) with vaginal estradiol valerate (2 mg twice daily). On day 10, ultrasound showed a triple-line endometrium measuring 9 mm with uterine dimensions increased to 6.7 × 3.5 × 3.1 cm.

Following confirmation of appropriate progesterone levels, a Frozen Embryo Transfer (FET) was performed with single blastocyst. Luteal support included vaginal progesterone (200 mg twice daily) and continued estradiol supplementation. She was additionally given Prednisolone 20mg once a day along with Aspirin 75 mg once daily. Prednisolone was tapered and stopped after 10 weeks of gestation. The patient achieved a clinical pregnancy, and delivered a healthy infant at 36 weeks of gestation.

The management of patients with multiple contributing factors to infertility should be comprehensive and individualized. A holistic approach begins with optimizing the body through antioxidant supplementation before initiating the ICSI/IVF process. Personalized treatment plans, including endometrial priming several cycles before embryo transfer, play a crucial role in enhancing implantation potential. Additionally, post-transfer support with aspirin and prednisolone can further improve outcomes. By integrating these strategies, successful pregnancy can be achieved even in complex infertility cases.

Discussion

CHH accounts for a minority of infertility cases in women but presents significant management challenges. Deficiency of GnRH secretion or pituitary responsiveness results in chronic hypoestrogenism, small ovarian size, and a hypoplastic uterus. Restoration of fertility requires exogenous gonadotropin therapy; however, these patients often need higher doses and longer stimulation periods due to limited follicular sensitivity. In this case, we used human menopausal gonadotrophin, providing both FSH and LH activity essential for follicular recruitment and estradiol production [3].

Hypoestrogenic states in CHH can result in poor uterine receptivity. Multiple cycles of progressive estrogen priming facilitated uterine enlargement and endometrial development, which are critical for implantation success. Sequential estrogen-progesterone therapy effectively simulated a natural cycle and achieved the desired endometrial pattern. An endometrial thickness of ≥ 8 mm with a triple-line pattern is often considered optimal for embryo transfer. Our patient achieved 9 mm, suggesting adequate estrogenization and vascularization.

The coexistence of SLE and Positive Antinuclear Antibodies (ANA) adds complexity to reproductive management. Autoimmune mechanisms can impair implantation and oocyte quality through inflammatory cytokines and oxidative stress. Studies suggest that ANA positivity is associated with lower implantation and pregnancy rates in ART cycles [4].

Pre-treatment with antioxidants and low-dose aspirin in our patient likely improved microcirculation and reduced oxidative damage, thereby enhancing embryo implantation. Importantly, disease stability was achieved before ART initiation through close rheumatologic monitoring, minimizing flare risks.

Reactive oxygen species (ROS) play a physiological role in folliculogenesis but, in excess, can lead to oxidative stress and damage oocyte competence. Studies have reported that supplementation with antioxidants such as Coenzyme Q10 (CoQ10) improves mitochondrial function and embryo quality, potentially increasing success rates in women with autoimmune or metabolic disorders [5].

Due to the absence of a natural LH surge, CHH patients have inadequate endogenous progesterone support. Therefore, exogenous progesterone is mandatory for luteal phase maintenance. Continuous estradiol supplementation further stabilizes the endometrium during early implantation. The combination used here effectively maintained progesterone and estrogen levels, supporting a successful gestation.

This case illustrates the critical importance of individualized ART protocols in complex infertility cases. Integration of hormonal, immunologic, and uterine factors ensured optimal follicular response and endometrial receptivity. The use of a multidisciplinary team, involving reproductive endocrinologists and rheumatologists, ensured safe fertility treatment without triggering autoimmune disease activity.

Conclusion

Congenital hypogonadotropic hypogonadism remains a rare but treatable cause of female infertility. This case demonstrates that with comprehensive pre-treatment, gradual hormonal priming, and tailored gonadotropin stimulation, successful conception is achievable.

Endometrial optimization and management of autoimmune factors were pivotal to the positive outcome. Personalized ART protocols-supported by multidisciplinary collaboration offer hope for favorable reproductive success in women with CHH and associated systemic disorders.

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