

Defying Expectations: A Rare Case of Hypergonadotropic Hypogonadic Pregnancy

SRIDIVYA CHERUKURI¹, KAMLESH CHAUDHARI², APOORVA DAVE³, SRAVYA GUDAPATI⁴



ABSTRACT

Amenorrhoea, hypoestrogenism, and hypergonadotropinism are the hallmarks of premature ovarian failure, affecting primary fertility in young females. Hypergonadotropic hypogonadism is a gonadal disorder that delays the onset of puberty in both males and females. In females, hypergonadotropic hypogonadism is also termed ‘Primary Ovarian Insufficiency’ (POI), which is characterised by premature ovarian failure. This is a rare case of a 27-year-old pregnant female with hypergonadotropic hypogonadism. She presented with primary infertility, and her laboratory investigations suggested hypergonadotropic hypogonadism or POI. Ultrasound imaging depicted a hypoplastic uterus with streak ovaries. She was treated with In-Vitro Fertilisation (IVF), which was successful on the second attempt. Hence, based on the findings of this case, it is recommended that females with POI should be counselled and informed about the small but real possibility of pregnancy.

Keywords: Amenorrhoea, Hypoestrogenism, Premature ovarian failure, Primary infertility, Primary ovarian insufficiency, Young females

CASE REPORT

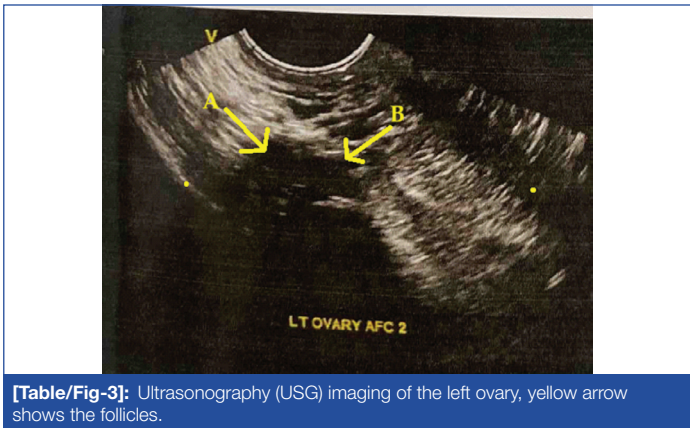
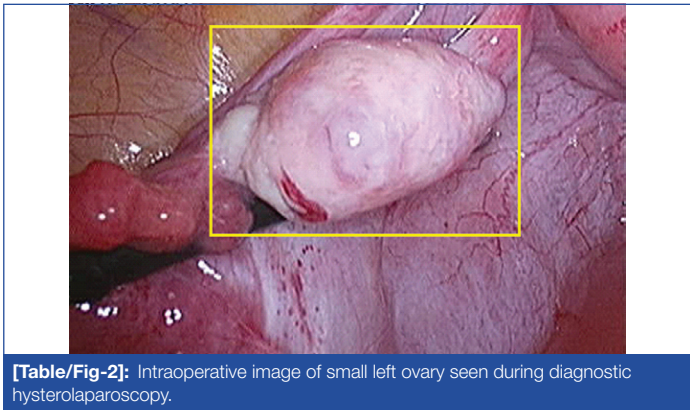
A 27-year-old married woman presented to the outpatient department with complaints of oligomenorrhoea and primary infertility for seven years. The patient achieved menarche at the age of 15 years, which was followed by irregular menstrual bleeding. There was no significant medical, family, or surgical history. The laboratory reports of the patient have been mentioned in [Table/Fig-1].

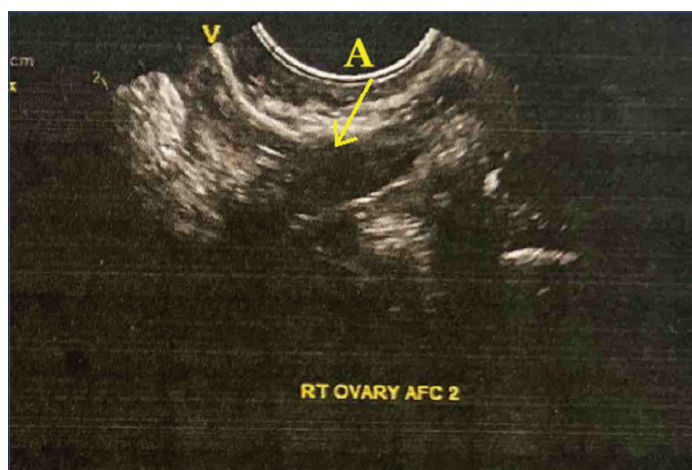
Parameter	Patient value	Normal range
17-OH Progesterone	0.46 ng/mL	0.1-0.8 ng/mL
Dehydroepiandrosterone sulphate	124.5 µg/dL	45-320 µg/dL
Estradiol	10 pg/mL	11-69 pg/mL
Follicle stimulating hormone	119.59 mIU/mL	3.5-12.5 mIU/mL
T3	3.40 pg/mL	1.74-4.1 pg/mL
T4	1.26 ng/dL	0.70-1.80 ng/dL
Thyroid Stimulating Hormone (TSH)	3.11 µIU/mL	0.30-5.5 µIU/mL
Glucose	92 mg/dL	70-100 mg/dL
Insulin (Fasting)	3.33 µU/mL	2.6-24.9 µU/mL
Luteinising hormone	51.62 mIU/mL	2.4-12.6 mIU/mL
Prolactin	9.31 ng/mL	2-29 ng/mL
Sex hormone binding globulin	61.69 nmol/L	26.1-110 nmol/L
Testosterone	28.2 ng/dL	11-70 ng/dL

[Table/Fig-1]: Laboratory profile of the patient.

Laboratory test results were suggestive of POI. She was scheduled for diagnostic hysterolaparoscopy, which revealed a small uterus with small ovaries [Table/Fig-2]. Based on the laboratory results and imaging, she was diagnosed with hypergonadotropic hypogonadism suggestive of premature ovarian failure. Ultrasound findings showed a right ovary measuring 1.8×1.5×1.0 cm with two small follicles observed, and a left ovary measuring 2.0×1.5×1.0 cm with two small follicles [Table/Fig-3,4]. The patient and her husband were counselled about the entire In-Vitro Fertilisation (IVF) process and informed about the success and failure rates as well. The treatment

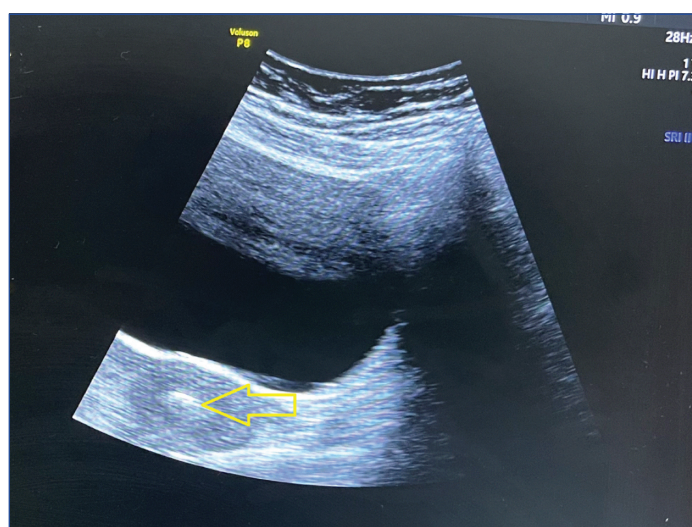
was initiated with a primary focus on regularising menstrual cycles. Later, she was prepared for ovulation induction using the long agonist method, followed by ovum aspiration. A total of 10 eggs were retrieved, which were later fertilised with her partner’s sperm. The fertilised ova were incubated for three days, and a 3-day embryo transfer was carried out, resulting in a successful pregnancy as evidenced by biochemical markers and clinical evaluation. Ultrasound imaging at a two-month follow-up showed a single intrauterine live embryo with a Crown-Rump Length (CRL)





[Table/Fig-4]: USG imaging of the right ovary, yellow arrow shows the follicles.

of 8.3 mm, corresponding to a gestational age of six weeks and five days [Table/Fig-5]. The patient delivered a healthy baby at the 36th gestational week.



[Table/Fig-5]: Small uterus with day 3 embryo in-situ.

DISCUSSION

Hypergonadotropic hypogonadism is characterised by increased gonadotropins and lower levels of sex hormones, leading to reproductive complications and POI. This condition primarily affects fertility in females [1]. POI is known to be linked to infertility in females, with one in 100 females under 40 years reported to be affected by it [2]. It presents clinically with symptoms such as hypoestrogenism, oligo/amenorrhoea, high gonadotropin levels, and decreased ovarian follicles, similar to menopause [2,3]. There are various underlying etiological factors responsible for causing POI, including autoimmune diseases, environmental factors, and genetic conditions such as fragile X syndrome and Turner syndrome [3]. The diagnosis of POI is usually unexpected and often part of other gynaecological problems.

Decreased bone density, increased susceptibility to cardiovascular diseases, cognitive disorders, menopausal symptoms, and depression have all been correlated with POI [4]. Unlike menopause, POI does not entail permanent ovarian failure, although ovulation is rare. The incidence of females with POI conceiving spontaneously is very low, reported at only around 1% of females under 40 years [5,6]. This case report discusses a 27-year-old female who presented with oligomenorrhoea and primary infertility and was diagnosed with a hypergonadotropic hypogonadic condition. She was managed with Assisted Reproductive Technology (ART) via the long agonist method and conceived successfully.

Hypergonadotropic hypogonadism, or POI, is typically diagnosed in relation to other gynaecological issues and can cause significant

emotional distress to both the patient and their family [6]. The number of mature follicles in the ovaries is greatly reduced, which is a major concern for patients with this diagnosis. This decreased number of follicles impacts fertility and must be addressed effectively [3,5]. There are sporadic case reports available on this condition, which relate to various genetic and other risk factors. One such factor is classic galactosaemia, which has been reported to affect the process of folliculogenesis by arresting the growth of follicles and inducing atresia [5-7].

Infertility can be managed with donated oocytes, which is also the recommended treatment for females with POI, offering higher success rates of between 70-80% [6]. Additionally, cryopreservation of follicles for fertility preservation has been recommended for patients with malignancies who are planned for treatment regimens that may cause gonadotoxic effects [8]. However, all these treatment modalities have limitations regarding availability and ethical concerns [6,7].

POI is characterised by reduced or intermittent ovarian functionality despite elevated levels of gonadotropins. The menopause-like condition in females affected by POI can be reversed, with ovarian function resuming in 20-24% of patients, and spontaneous pregnancy can be achieved in about 5% of patients [6,9]. The resumption of ovarian functionality can depend on multiple factors, including the nature of amenorrhoea. One research study reported that less severe mechanisms were associated with secondary amenorrhoea compared to primary amenorrhoea [9].

Conte FA et al., reported a case of pseudohermaphroditism with aromatase deficiency characterised by high levels of testosterone; however, in contrast, the patient in this case exhibited normal secondary sexual characteristics within the normal limits of testosterone [10]. Menezo YJ et al., mentioned a case involving galactosaemia and high Follicle Stimulating Hormone (FSH), which is a known cause of POI. In this particular patient, however, this was not observed, suggesting potential clinical variations [11].

Restoration of estrogen levels can be beneficial in managing associated clinical symptoms such as maintaining bone density, cognitive functionality, and addressing complications arising from autoimmune mechanisms, thus contributing to overall health status. Recommendations suggest maintaining estradiol levels at 100 pg/mL per day to aid in resuming ovarian function [5]. Hormonal replacement therapy is recommended, and there have been reports of achieving spontaneous pregnancy as noted by Calik-Ksepka A et al., However, this may not be effective in all cases, as observed in this case [6]. Therefore, a decision was made to proceed with IVF. While there are various management recommendations, spontaneous pregnancy success rates remain very low. Although rare, there are still chances of achieving pregnancy [1,5], as noted in this case. This patient was counselled accordingly and managed through IVF.

CONCLUSION(S)

Hypergonadotropic hypogonadism can result in amenorrhoea in younger females and affect fertility. A better understanding of the multiple underlying pathophysiological factors associated with this condition necessitates further research. Although rare, there are chances of successful conception and delivery.

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PARTICULARS OF CONTRIBUTORS:

1.

Junior Resident, Department of Obstetrics and Gynaecology, Jawaharlal Nehru Medical College, DMIHER, Sawangi, Meghe, Wardha, Maharashtra, India.
2.

Professor, Department of Obstetrics and Gynaecology, Jawaharlal Nehru Medical College, DMIHER, Sawangi, Meghe, Wardha, Maharashtra, India.
3.

Associate Professor, Department of Obstetrics and Gynaecology, Jawaharlal Nehru Medical College, DMIHER, Sawangi, Meghe, Wardha, Maharashtra, India.
4.

Senior Resident, Department of Obstetrics and Gynaecology, Jawaharlal Nehru Medical College, DMIHER, Sawangi, Meghe, Wardha, Maharashtra, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Sridivya Cherukuri,
Junior Resident, Department of Obstetrics and Gynaecology, Jawaharlal Nehru Medical College, DMIHER, Sawangi, Meghe, Wardha-442004, Maharashtra, India.
E-mail: divyacherukuri27@gmail.com

PLAGIARISM CHECKING METHODS: [\[Jain H et al.\]](#)

- Plagiarism X-checker: Dec 20, 2024
- Manual Googling: Mar 27, 2025
- iThenticate Software: Mar 29, 2025 (2%)

ETYMOLOGY: Author Origin

EMENDATIONS: 6

AUTHOR DECLARATION:

- Financial or Other Competing Interests: None
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. Yes

Date of Submission: [Dec 19, 2024](#)
Date of Peer Review: [Feb 06, 2025](#)
Date of Acceptance: [Mar 31, 2025](#)
Date of Publishing: [Sep 01, 2025](#)