Case Report

# IUI in hypogonadotropic hypogonadism: Do not give up

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## ABSTRACT

Ovulation is dependent on the presence of a functioning hypothalamic-pituitary-ovarian (HPO) axis. Estimates of chronic anovulation rates range from 6-15% of women during the reproductive years.Potential causes of anovulation are PCOS, hyperprolactinemia,thyroid dysfunction, stress etc. Idiopathic hypogonadotropichypogonadism (IHH) is rare cause of anovulation. Idiopathic hypogonadotropichypogonadism (IHH) is a collection of genetic mutations that result in delay of puberty, infertility, and low gonadotropins.Women with IHH have hypoestrogenism, amenorrhea, and low gonadotropin levels. Ovulation induction is the method for treating anovulatory infertility. For patients with hypogonadotrophichypogonadism, the treatment involves administration of both FSH and LH, while HCG is injected for follicle rupture. Such patients need high dosage and longer duration of stimulation than other patients.

**Keywords:** Hypogonadotropic hypogonadism (HH), intrauterine insemination (IUI), ovulation induction

## INTRODUCTION

Hypogonadotropic hypogonadism (HH) has been classified by the World Health Organization (WHO) as a group 1 anovulation disorder.[1] HH is usually idiopathic with no anatomical lesions in the hypothalamo-pituitary tract[2] and is characterized by amenorrhea, hypoestrogenism, low serum gonadotropins, and a broad spectrum of abnormal secretion patterns of hypothalamic gonadotropin-releasing hormone (GnRH).[3,4]

Several etiologic factors have been described for idiopathic HH including intense or frequent exercise, weight loss, psychological stress, and psychological disturbances.[5-8]

In addition to being infertile, women with HH suffer from conditions associated with a low estrogenic milieu, including osteopenia.

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Of all the causes of infertility, HH is the least common etiology. Patients in whom fertility is desired, induction of gonadotropin secretion by pulsatile GnRH or treatment with exogenous gonadotropin is the current treatment of choice.[9-11] The average treatment duration and the number of ampules used are higher compared with patients with other etiologies of infertility. This may be explained by the "dormant" ovaries that need to be primed before follicular response is achieved. Hence, the question arises about the dose from which to start stimulation and about when the lack of potential response can be defined.

We present a case that illustrates the concept that using a high human menopausal gonadotropin (hMG) dose for an unusually long time may be rewarding.

## CASE REPORT

A 28-year-old lady was referred as a case of primary infertility with secondary amenorrhea for assisted reproductive technology (ART). Hypogonadotropic hypogonadism (HH) was diagnosed during the evaluation of secondary amenorrhea. Investigations



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revealed a small uterus with normal ovaries on laparoscopy, follicle-stimulating hormone (FSH) of 0.39 mIU/mL and luteinizing hormone (LH) of 0.74 mIU/mL and her serum prolactin and thyroid-stimulating hormone (TSH) to be within normal limits. Karyotype analysis revealed a pericentric inversion of chromosome 2 (estimated to occur in up to 1% of the population, probably without clinical relevance to HH). The patient was completely evaluated for the cause of adult-onset idiopathic HH but we could not come to any conclusion. Her body mass index (BMI) was low (weight: 36 kg; BMI: 15.2 kg/m$^2$) and psychogenic stress could not be ruled out. Before her referral, repeated attempts of ovulation induction were attempted in the last 5 years. All inductions were cancelled due to nonresponsiveness of the ovaries. The patient's husband had a sperm concentration of 60 million/mL with a progressive motility (PR) of 50%. The patient was started on human menopausal gonadotropin (hMG) injection at a dosage of 75 IU/day on the second day of her menstrual cycle and the dose was gradually increased to a maximum of 225 IU/day. She received a total dose of 3,750 IU over 18 days. A single follicle of 1.9 cm developed on the right side and the endometrial thickness was 8 mm. Ovulation was triggered with 10,000 IU of human chorionic gonadotropin (hCG) and intrauterine insemination (IUI) was done 36 h later. IUI resulted in a singleton clinical pregnancy.

## DISCUSSION

The prognosis of inducing ovulation in patients of HH is favorable though they require high doses of hMG. The baseline FSH and LH values do not predict an individual patient's response to hMG. The patient's response can be judged only after the patient is subjected to stimulation by ultrasonography (USG).

An unfavorable response to hMG stimulation was achieved in our patient prior to ovulation induction protocol due to the low dose of hMG.

We should know how high a dose of hMG to give and for how long to give this dose before we give up. In a patient of HH after head trauma, Ferrari and Crosignani[12] used massive doses of hMG therapy before giving up. Our current case report clearly illustrates that in these specific groups of patients, it is worthwhile to go to extremes with regard to treatment duration and dose. In patients with HH, the threshold for ovarian response may differ substantially from one patient to another.

In one case report by Dragojevic *et al.*,[13] hMG injection was used for follicular development in a 38-year-old patient of HH with empty sella syndrome that led to the formation of two follicles and after IUI, resulted in a successful singleton pregnancy and subsequent live birth.

In another case report, successful twin pregnancy was achieved in a 36-year-old patient of primary HH with empty sella syndrome after using recombinant FSH and LH.[14]

We conclude that patients with HH undergoing ovarian stimulation for *in vitro* fertilization (IVF) should be carefully assessed, on a trial and error basis, for ovarian response before we give up.

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### Conflicts of interest
There are no conflicts of interest.

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