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Case Report

Hypogonadotropic Hypogonadism: Can have Multiple Pregnancy and or Ovarian Hyper Stimulation Syndrome

Nisreen Aref Albezrah*

Head of Obstetric and Gynecology Department, Taif University, Saudi Arabia

***Corresponding author:** Nisreen Aref Albezrah, Head of Obstetric and Gynecology Department, Taif University, Saudi Arabia

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Abstract

Hypogonadotropic hypogonadism (HH) is the least common etiology of all the causes of infertility. Patients in whom fertility is desired, induction of gonadotropin secretion by pulsatile GnRH or treatment with exogenous gonadotropin is the current treatment of choice. Ovulation induction in patients with hypogonadotropic hypogonadism (HH) is a challenge to the treating physician.

The ovarian response in HH cannot be predicted and may differ substantially from that of normal patients. A step-up protocol longer duration of stimulation is required in some cases to reach that threshold levels of follicle stimulating hormone, in so as to prevent multiple pregnancies and to eliminate the risk of ovarian hyper stimulation syndrome (OHSS).

Keywords: Ovarian hyperstimulation syndrome; Hypogonadotropic hypogonadism; Ovulation induction

Introduction

Hypogonadotropic hypogonadism (HH) is a rare cause of infertility, characterized by reduced hypothalamic or pituitary activity resulting in abnormally low serum FSH and LH levels and negligible estrogen activity and has classified as a group 1 anovulation disorder by World Health Organization (WHO) [1-4].

Irrespective of the underlying etiology, women with HH require both LH and FSH to restore normal ovarian function and override follicular growth arrest which can be achieved by either exogenous gonadotropins or pulsatile GnRH pump [5]. The average treatment duration and the number of ampules used for HH patients are higher compared with patients with other etiologies of infertility and the ovarian response in these patients may differ substantially from that established for normal patients. The success of ovulation induction is reported to be as high 60–80% with a high multiple pregnancy rate (20–50%) [6].

In order to avoid higher order pregnancies, these patients may require a longer duration of stimulation with gradually stepping up the dose in order to reach the threshold of FSH and LH [7]. Moreover assisted reproductive technology (ART) is beneficial in this group of patients to prevent higher order multiple pregnancies or to increase the chance of pregnancy whenever there is a poor response on ovarian stimulation but OHSS and multiple pregnancies still can happen and each patient should be assessed carefully and individually. We present a case with hypogonadotropic hypogonadism who developed OHSS and multifetal pregnancy after controlled ovulation-stimulating and IUI with human menopausal gonadotrophin (HMG) and human chorionic gonadotrophin (HCG).

Case Report

Mrs. S.A.N, 29-year-old, was referred to as a case of primary amenorrhea with primary infertility for 3 years to Maternity and Child Hospital in Taif city / Saudi Arabia. She had not attained her menarche by 17 years of age and gave a history of withdrawal bleeding on combined oral pills only (E+P). During the evaluation of primary infertility, HH was diagnosed. Her serum hormone measurements determined the following results; follicle stimulating hormone (FSH) -0.124mIU/ml, luteinizing hormone (LH) -0.185mIU/ml, estradiol- 7pg/ml and her serum thyroid stimulating hormone (TSH) and serum prolactin was within normal limits. Body mass index (BMI) was normal (20.2kg/m^2) and psychogenic stress could not be ruled out. Hysterosalpingography showed blocked lift fallopian tube. The husband's semen analysis was normal. Before her referral, repeated attempts of ovulation induction were attempted in a private clinic in the last three years. All inductions were canceled due to poor responsiveness of the ovaries. In a private clinic, ovarian stimulations had commenced by

Clomiphene Citrate (CC)150 mg for 3 cycles with no response when she was started on Menagon, (HMG, Ferring Pharmaceuticals) 150 IU for 12 days in one cycle and Gonal F Gonal-f® (follitropin alfa for injection. Merck Sorono) 300IU for 15 days in the second cycle , however pregnancy was not achieved . In our clinic Controlled ovarian hyper stimulation (COH) and IUI was planned, Menagon 225 IU was started on the second day of the cycle (3 amp per day for 16 days). A transvaginal scan was done on day 7, 9, 12. 14 and on day 16, it showed 2 follicles (17mm and 18mm in diameter). 10000 IU h-CG (Pregnyl 5000 IU amp. Organon) was given by intramuscular (IM) injection on treatment day 17, Swim-up and Percoll gradients were indiscriminately employed for insemination using her husband's sperm. Intrauterine insemination was performed 36 h after IM hCG administration. The luteal phase was supported with 100mg/day micronized progesterone (Progestan 200mg, KocakFarma) however she got her period after 14 days from HCG injection. COH Controlled was repeated using Menagon 300 iu (4 ampules/day) for 12 days which was followed by vaginal scan on day 7,9,11, and the last scan on day 14 showed 3 dominant follicles with size 16,17 and 18mm in diameter in each ovary. IUI done based on the patient request and insist despite the risk of OHSS was explained. The patient was using Folic Acid, Aspirin, and cyclogest suppository. The pregnancy test was positive after 7 days of missing her period.

At 6 week, the scan showed five intrauterine gestational sacs. Both ovaries are enlarged with 5-6 cysts (30-50 mm in diameter with fluid behind the uterus and renal angles. Her vital signs were stable. Liver function (LF), renal function (RF) and coagulation profile were all normal. She was advised for admission but refused and signed. She came back after one week to the emergency room with mild abdominal pain. Her vital signs were stable. Lung examination is normal. Her abdomen was mildly distended below the umbilicus. The scan showed five intrauterine viable fetuses, both ovaries enlarge (10 by 7cm and 9 by 8 in diameter) with multiple follicles (40-50mm in diameter) with evidence of ascites. She was diagnosed as a case of multiple pregnancies with moderate ovarian hyperstimulation syndrome (OHSS), admitted to the gynecology ward under close observation and managed according to OHSS protocol. Her renal function (RF), liver function test (LFT) and coagulation profile were normal. Pt refused albumin infusion and discharged home after 24 of admission. She was referred to Assisted Reproductive Unit (ART) in another hospital for embryo reduction which was done for 3 embryos successfully after which she was following regularly in a Feto-Maternal unit in a private hospital for her pregnancy.

Discussion

HH is one of reproductive function disorders which is rare and characterized by the absence of normal hypothalamic-pituitary synchronous activity. These patients belong to WHO Group 1 anovulation which accounts for 10% of cases for anovulation and present with the history of amenorrhea, hypogonadism [8] and low gonadotropin.

The response of an individual patient to gonadotropin treatment in HH cannot be predicted and is not based on baseline LH and FSH estimation, which we usually use for other patients. AMH may be useful to some extent. [9] Ovaries may or may not be seen on USG in these patients. Patients need to be subjected to gonadotropin stimulation after which we can estimate her pattern of response. Patients with HH have threshold for ovarian response may differ substantially from that established for a normal patient.

The accepted and recommended treatment method for patients with HH is ovulation induction by gonadotrophin drugs. In such patients, optimal clinical results are achieved by using FSH combined with LH, [10] which is accomplished by administration of HMG, recombinant LH or low dose human chorionic gonadotropin. The most frequent complications of ovulation induction with gonadotropin in these patients are OHSS and Multifetal pregnancy which are serious and potentially life-threatening. One should bear in mind that this is not a homogeneous group and an individual approach for ovulation induction should be applied in order to decrease the incidence these complications and if a step-up protocol is used to decrease the incidence of multiple pregnancies, it will lead a longer duration of stimulation.

Our case emphasizes that OHSS and multiple pregnancies can be seen in patients with HH after ovulation induction with HMG and IUI who was stimulated before two times and failed to respond. We should know how high a dose of hMG to give and for how long to give this dose before give up or end in up in risk of complication.

We conclude that patients with HH undergoing ovarian stimulation for IVF should be carefully assessed, on a trial and error basis, for the ovarian response before we give up on obtaining fertilizable oocytes. Ovarian reserve is difficult to assess in these patients and very little information is available on the high-risk groups and prophylaxis of OHSS in HH patients .When planned for ovulation induction we must be prepared for a longer duration of stimulation which does not affect the quality of oocytes and embryo and the pregnancy rate. The treating physician and the patient need a lot of patience and motivation to continue the treatment for a longer duration. And counseling for the complication should always be explained and stressed.

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