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Successful controlled ovarian stimulation and pregnancy in a woman with hypogonadotropic hypogonadism resulting from transsphenoidal excision of a pituitary macroadenoma

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Abstract

Introduction: To report pregnancy in women with partial hypopituitarism as a result of surgery for a non-functioning pituitary macroadenoma using recombinant Follicle Stimulation Hormone (rFSH) and Recombinant Luteinizing Hormone (rLH).

Case Description: A 29-year-old woman with partial hypopituitarism underwent Controlled Ovarian Hyperstimulation (COH) with rFSH, rLH achieving a pregnancy. Co-treatment with rLH enhanced FSH action, promoted follicle development and shortened COH duration and reduced FSH doses.

Conclusion: Ovulation induction in women with partial hypopituitarism requires both Follicle Stimulation Hormone (FSH) and Luteinizing Hormone (LH) to achieve optimal follicular growth. Adding LH from start of stimulation optimizes controlled ovarian stimulation in hypogonadotropic hypogonadism supporting the concept that LH is required in the early follicular phase as well.

Keywords: Controlled Ovarian Hyperstimulation (COH); Luteinizing hormone; IVF/ET; Partial hypopituitarism

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Introduction

Hypogonadotropic hypogonadism (HH) is one of the least common etiology for female infertility, although treatment in most cases leads to successful conception. These patients often are prescribed human menopausal gonadotropin (HMG).[(1)] To achieve adequate Ovulation Induction (OI), the average treatment duration and the doses of gonadotropins used are higher compared to patients with other etiology of infertility.[(2)] A significant proportion of hypogonadotropic patients do not appear to have the minimum amounts of endogenous LH required to achieve optimal follicular development and steroidogenesis.[(3-4)] Findings from our case study indicated that LH activity is compulsory in COH for hypogonadotropic hypogonadism patients.

Case Report

29- year old lady was previously diagnosed to have a non-functioning pituitary macroadenoma at the age of 23 years. She had undergone transsphenoidal excision of the tumor at another center. After that, she developed central hypothyroidism and hypogonadotropic hypogonadism. She was on replacement therapy with L-Thyroxine. She attended clinic as she desired of pregnancy and her clinical examination was unremarkable. Her hormonal profile was as follows: serum Prolactin 6.27ng / ml (5 - 25 ng /ml), serum Thyroid Stimulating Hormone (TSH) - 0.092 µIU/ ml (0.3 - 4.5 µIU/ml), serum luteinizing hormone (LH) - 0.15 mIU/ml (follicular phase & luteal phase 0.5 - 18 mIU/ml), serum Follicle stimulating hormone (FSH) - 0.37 mIU/ml (follicular phase 3.9 -10; luteal phase 2.3 - 8 mIU/ml).

When Patient came to our center, she was amenorrheic for three months as she had periods only after taking medications. Oral contraceptive pill and tab Progynova 2 mg twice a day was given to assess the endometrium, which was good triple layered 8mm after 20 days of estrogen intake. Controlled ovarian stimulation was started on day 2 of the period with daily subcutaneous injections of 300 IU rFSH for 11 days, 75 IU rLH for 11 days. Baseline serum FSH, LH, E2 were <0.3 mIU/ml. <0.07 mIU/ml and 14.6 pg/ml.

On the day of ovulation trigger, her E2 level was 4079.4 pg/ml, and progesterone was 0.9ng/ml. Ten follicles of 16 mm, two follicles of 12 mm and three follicles of 9 mm were recruited. The endometrial thickness was 11mm. 250 mcg of hCG was administered on stimulation day 12 for final oocyte maturation, and oocyte pick-up was performed 36 hours later. The total dose of 3300 IU rFSH, 825 IU LH were administered. Nine oocytes were retrieved and two blastocysts transferred, rest three blastocysts were frozen. Two weeks after embryo transfer, serum b-HCG level was 1200mIU/ml.

Discussion

Until recently, for women with hypogonadotropic hypogonadism undergoing ovulation induction with gonadotrophins, human menopausal gonadotrophin (HMG), was the only source of exogenous LH. The relatively high number of HMG ampules needed to induce ovulation in an HH female patient was well

documented.[2] However, the prognosis for inducing ovulation in these patients is favorable. The prediction of an individual patient to respond to hMG treatment cannot be made on baseline LH and FSH levels, which we usually use for other patients. Only after starting a patient on such treatment we can estimate her pattern of response.

In a case report by Lewis N et al. after 20 stimulation days (120 ampules of HMG), a single oocyte was retrieved and fertilized by intracytoplasmic sperm injection (ICSI), and a four-cell embryo was replaced; however, only "biochemical" pregnancy was achieved.[1]

In the case report by Koji Nakagawa et al an initial dose started was, 75 IU of hMG, which was continued for the 14 days because adequate follicular development was not achieved. Then dose of hMG was increased to 150 IU for the next seven days. Two follicles had developed after 22 days from the start of stimulation. Pregnancy was achieved and delivered a male infant weighing 830 gm at 27 weeks of gestation due to uncontrolled blood pressure.5

The treatment of hypogonadotropic women with urinary FSH or rFSH alone resulted in a much higher requirement of gonadotropin, slower follicular development, lower serum estrogen level, and fewer mature follicles.[6-7] The above findings are supporting the recent concepts of gonadotrophic control of follicular growth and function.[8-9] It indicates that for normal follicular development induced by FSH also, optimum LH is required to induce ovulation. rLH is an ideal adjunct therapy to rFSH in hypogonadotropic anovulation. The administration of rLH in association with rFSH in WHO group I anovulatory women is documented as safe and effective in some case reports.[10-11]

In a case report of a woman with Kallman syndrome , by E.Kousta et al. , used rFSH 150 IU and rLH 225IU for ovulation induction. After nine days of stimulation 10,000 IU of HCG was given for ovulation. Pregnancy confirmed on transvaginal ultrasonography and resulted in delivery of female infant 3096 gm by cesarean section.[12]

A study was carried out in Spain by "Burgués and the Spanish Collaborative Group on Female Hypogonadotrophic Hypogonadism, in which 38 women with hypogonadotropic hypogonadism (WHO group I) were included. Patients were started on 150 IU/day rFSH and 75 IU/day rLH (with the possibility of dose adjustment) as a single S.C. injection for up to three cycles. The total number treatment cycles was 84. Adequate follicular growth was seen in 94% out of 84 initiated cycles. In most of the treatment cycles (94%), 75 IU rLH dose was found to be effective. The average duration of stimulation was12.2 days. Pregnancy was achieved in 15 of the 38 patients (39.5%). This study concluded that rFSH along with rLH induces follicular growth, ovulation, and pregnancy in a good proportion of hypogonadotropic anovulatory patients. The most appropriate doses were150 IU rFSH and 75 IU rLH.[13]

In our case, we also found that addition of 75IU of rLH along with rFSH 150 IU resulted in shorter stimulation days(11days), more follicular recruitment, the good number of oocytes retrieved (10 MII), good fertilization and pregnancy was achieved which is ongoing presently at 14 weeks.

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