

Successful pregnancy despite advanced age and elevated serum follicle stimulating hormone levels - A case report

J. H. Check

The University of Medicine and Dentistry of New Jersey, Robert Wood Johnson Medical School at Camden, Cooper Hospital/University Medical Center, Department of Obstetrics and Gynecology, Division of Reproductive Endocrinology & Infertility, Camden, New Jersey (USA)

Summary

Purpose: To determine if a woman over age 45 with elevated serum follicle stimulating hormone (FSH) levels in the early follicular phase could still successfully conceive.

Methods: Female partner was treated with guaifenesin to improve cervical mucus quality and vaginal progesterone in the luteal phase. Careful monitoring of follicular maturation was performed.

Results: A successful pregnancy after 14 months of progesterone therapy was achieved.

Conclusions: It is possible for a 46-year-old infertile woman with elevated serum FSH to achieve a pregnancy even when the male partner is taking calcium channel blockers for heart problems.

Key words: Elevated FSH; Advanced age; Calcium channel blocker.

Introduction

It has been estimated that in the general population the decline in fecundity accelerates between 35 and 40 years of age and approaches zero by age 45 [1]. Some studies have concluded that at any age an elevated serum follicle stimulating hormone (FSH) in the early follicular phase forebodes a poor prognosis [2-8]. One in vivo study of elevated early follicular phase serum FSH levels did not conclude such an ominous prognosis for women age 39 or younger but did conclude a very poor viable pregnancy rate (PR) for women 40 or above [9]. Other adverse factors include a short follicular phase related to early follicular recruitment [4, 10].

It is not clear whether the paucity of documented cases of pregnancies in women over age 45 who have conceived might be a select group that has had a lower rate of atresia than most age matched peers. Possibly, had serum FSH been measured in the early follicular phase, they could possibly be distinguished by normal serum FSH and have possibly normal length follicular phases. The majority of these women may have conceived spontaneously so these types of studies are not available.

A case report is described where a 46-year-old infertile woman conceived following treatment despite elevated early follicular phase serum FSH levels and shortened follicular phases.

Case Report

A 45-year-old woman presented for infertility management. She had been trying for 15 months without success with her second husband. She had conceived twice at age 34 with her first husband, but both pregnancies ended in early first trimester spontaneous abortions. Her 39-year-old husband fathered two

children in his first marriage, the youngest age 11. He had a myocardial infarction at age 32 and he was taking diltiazem hydrochloride, a calcium channel blocker, at 300 mg/day plus simvastatin and quinapril hydrochloride.

The female partner had a hysterosalpingogram eight years before by a reproductive endocrinologist because of her difficulty in conceiving then ending in spontaneous abortion. She had at least 8 cycles of clomiphene citrate with 5 cycles of intrauterine insemination but never conceived.

The female partner was still having regular menses 26-30 days apart. She was monitored by serial pelvic ultrasound and hormonal studies (estradiol [E2], progesterone [P], and LH). Though she attained a serum E2 level of 267 by day 15 of her first cycle of investigation, she formed two follicles with maximum sizes of 14.3 mm and 15.7 mm when the LH rose.

She was then treated with guaifenesin [11] and ethinyl estradiol (20 micrograms per day) from day 3 of her cycle combined with 75 IU human menopausal gonadotropin (hMG) beginning day 5 of the cycle [12]. The post-coital test improved and the average diameter of the dominant follicle reached 20 mm and the peak serum E2 was 229 pg/mL. After oocyte release documented by sonography she was supported with P vaginal suppositories 100 mg twice daily.

The patient skipped 3 cycles and came in on day 10 with no medication so the post-coital test was poor as before. She was given 10,000 U of hCG and had intrauterine insemination 40 hours later but the oocyte did not appear to release by sonography. The patient then finally consented to another hysterosalpingogram which was completely normal.

Because of expenses with hMG another technique was tried where the patient used ethinyl estradiol 20 micrograms days 2-8 then took clomiphene citrate 100 mg days 9-13 and then resumed ethinyl estradiol 20 micrograms daily. She attained a 21.6 mm follicle on day 19 with a serum E2 of 447 pg/mL. The follicle showed oocyte release 40 hours later and intrauterine insemination was performed.

Eight months after her initial appointment for the first time her FSH was increased on day 3 (11.2 mIU/mL with a serum E2 of 57 pg/mL. In that cycle she attained a 20.3 mm follicle and serum E2 of 255 pg/mL by day 10 without any therapy. Intrauterine insemination was performed. The patient attained

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mature follicles without the use of follicle maturing drugs for several consecutive cycles, but earlier – at day 9 or 10 – and because of fair post-coital tests on guaifenesin therapy alone, no IUIs were performed. The only additional therapy was progesterone in the luteal phase.

During the 13-month treatment course the patient had serum FSH measured on day 3, several times. The highest level recorded during this 13-month time period was 23.6 mIU/mL and the next highest was 22.7 mIU/mL. The lowest level was 16.1 mIU/mL.

The patient conceived on her 14th month of progesterone therapy at age 46. She successfully completed her first trimester. Chorionic villus sampling showed a normal female fetus.

Discussion

There is evidence that with advancing reproductive age the main limiting factor in humans is an oocyte factor especially related to aneuploidy [13, 14]. The case described herein indicates that the possibility of successful pregnancy is at least possible in a woman aged 46 with elevated early follicular phase serum FSH and early follicular recruitment. Though we cannot prove it, we believe progesterone supplementation in the luteal phase is essential. Previous data supports not using follicle maturing drugs but only using luteal phase progesterone support when there is adequate follicular maturation [15]. In fact, the use of follicle maturing drugs in a woman with advanced reproductive age and increased FSH can iatrogenically create a state of hypergonadotropic hypogonadism and amenorrhea that is reversible upon stopping the follicle maturing drugs [16]. This may be related to the further increase in FSH causing down regulation of its own receptor [17].

This case was further complicated by the fact that the woman's husband was taking calcium channel blockers. There have been reports that the use of these types of drugs causes a defect in the ability to increase the percentage of spermatozoa with plasma membrane mannose-ligand receptor expression over the acrosome and post-acrosomal regions of the sperm head, and the percentage of spermatozoa exhibiting spontaneous and mannose-induced acrosome reaction following incubation of spermatozoa under standard capacitating conditions [18-20]. The authors thus stated that these agents would cause infertility in almost all males taking these drugs [20]. In fact, these agents are being touted as potential male contraceptives. However, since this concept has been challenged and many cases of successful pregnancy have been reported despite the male taking these drugs [21], we elected not to ask his internist to change his medications since they were believed to be essential for his good health. Furthermore, we did not think that the patient's prognosis for conception was good enough to warrant her husband taking a health risk. He confirmed that he was on the same dosage of calcium channel blockers when his wife conceived. Thus, this case confirms that conception despite ingestion of calcium channel blockers by the male partner is very possible. Perhaps some calcium channel blockers, but not others, will be found to reduce male fertility.

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Address reprint requests to:
 JEROME H. CHECK, M.D., Ph.D.
 7447 Old York Road
 Melrose Park, PA 19027 (USA)