

Oligospermia In A Man With Small Testes And Elevated Serum FSH Responds To Low Dose Estrogen-Testosterone Combination Therapy, Resulting In His Wife's Pregnancy And Live Birth

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Citation

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Abstract

Oligospermia due to small testes with elevated serum FSH is a condition that is usually considered as untreatable. These men require assisted reproduction to overcome their infertility, but this is not a cure for their oligospermia. We present the case report of a man who had oligospermia with small testes and elevated serum FSH. He was treated with low dose oestrogen-testosterone combination therapy. His sperm count increased, serum FSH level became normal, and his wife conceived spontaneously within two months of starting the treatment.

INTRODUCTION

Oligospermia is defined as a sperm count of less than 20×10^6 per mL, it has different etiologies. However, in most of the cases the cause cannot be determined, and it is then considered idiopathic. Several empirical therapies are available for this type of oligospermia. However, oligospermia due to small testes with elevated serum FSH is a condition that is difficult to treat (Abyholm, 1983). We present the case report of such a man whose sperm count increased after receiving low dose estrogen-testosterone combination therapy, and whose wife conceived spontaneously.

CASE REPORT

A 30-year-old infertile man, married for four years, attended the private clinic on November 15, 2004. Semen analyses (SA), performed eight times between November 26, 2001 and November 15, 2004 showed a sperm count (C) of $2 - 10 \times 10^6$ per mL (mean 3.8×10^6 per mL), sperm motility (M) at one hour 1- 10 % (mean 6%) and normal sperm morphology (N) less than ten percent. The volumes of the ejaculates were always normal, and bacterial cultures of the semen showed no growth of any microorganisms on two occasions.

He had received hCG, mesterolone, and clomiphene between December 2001 and May 2003, but the sperm counts did not

improve. He last received medical therapy in May 2003. The couple had a failed attempt at IVF in early 2004.

The patient did not have a past history of any significant illness or sexual dysfunction, nor had he a history of being exposed to heat or chemicals. He reported no addiction. He had a family history of infertility, his maternal uncle and elder brother were both infertile, but their medical records were not available. Karyotyping was not done because he refused the test due to cost, and because of lack of treatment for any abnormality that might have been detected.

He was normotensive and nondiabetic. On physical examination: he was androgenized without gynecomastia; his testes were of normal consistency, but small in size, there was no evidence of any varicocele or any epididymitis.

Hormone assays done on July 10, 2003 showed normal serum TSH and PRL, but elevated serum FSH (15.1 mIU/mL, normal range was 1.0-12.0 mIU/mL). Before starting the treatment on November 15, 2004, his serum FSH was elevated (15.4 mIU/mL, normal range was 1.7-12.0 mIU/mL), serum testosterone was at the upper normal limit (10.1 ng/mL, normal range was 3-10 ng/mL) and serum estradiol was elevated (93.6 pg/mL, normal upper limit was up to 65.0 pg/mL). Scrotal ultrasonography revealed small testes (right one was of 5.0 mL and the left was of 5.4 mL in

volume). The echopattern of testes was normal without evidence of tumor, varicocele or epididymitis.

After taking written informed consent, and without giving any assurance of a cure, the patient was given one combination tablet of ethinyl estradiol 0.0044 mg and methyl testosterone 3.6 mg orally daily, starting November 18, 2004.

On January 31, 2005, seventy-four days after starting of the treatment, his SA showed: C- 25pregnancyx10⁶ per mL, M- 15 % and N-15 %. The patient did not report of any adverse effects and no problems were detected upon physical examination. Hormone assays performed at that time showed normal serum FSH (9.1 mIU/mL, normal range was 1.7-12.0 mIU/mL), serum testosterone (5.6 ng/mL, normal range was 3-10 ng/mL) and serum estradiol (59.8 pg/mL, normal upper limit was up to 60.0 pg/mL). Scrotal ultrasonography did not show any changes in the size or echopattern of the testes (right one was of 5.0 mL and the left was of 5.5 mL in volume), and no evidence of tumors was seen.

The patient's wife had her last menstruation on December 24, 2004 and on February 12, 2005 her pelvic ultrasonography showed a live intrauterine singleton pregnancy of seven weeks. She delivered a boy weighing 2800 grams by caesarean section on September 2, 2005

DISCUSSION

The patient had infertility with oligospermia and small testes. No testicular biopsy was performed, because it is usually not required in men with small testes and elevated serum FSH (Sigman and Howards, 1992). He had elevated serum FSH, serum testosterone at the upper normal limit, and elevated serum estradiol before starting of the low dose estrogen-testosterone combination therapy. Serum LH was not assayed; a study of infertile men with sperm count of less than 10X10⁶ per mL indicated that measurement of serum testosterone and FSH alone will detect the majority of testicular endocrine abnormalities (Sigman and Jarow 1998). He had small testes, 5.0 and 5.4 mL in volume [minimum testicular volume is more than 15mL, although ethnic differences exist (Diamond 1986)]. Sperm counts decrease, and FSH levels increase, in accordance with decreasing testicular volume (Bujan et al., 1989). Thus, his low sperm count was probably related to his reduced testicular volume, and consequently serum FSH was elevated. This elevation in FSH in turn probably resulted in increased aromatization of

testosterone to estrogen (Kula and Chilarski 1987). In an earlier report (Sah 1998), we have hypothesized that low dose estrogen-testosterone combination therapy may act directly on the seminiferous tubules. This may be the case in this patient. By normalizing the sperm count, this therapy restored FSH to normal levels, and consequently normalized those of estradiol. Furthermore, a man with oligospermia due to 'partial maturation arrest', was shown to increase his sperm count after receiving the same therapy, being able to impregnated his wife (Sah 2002).

This report differs from our two earlier reports in that, the patients in the previous reports had normal testicular volumes, and their hormone profiles were not known. Whereas the patient in this report had small testes, and the effect of the therapy on his hormonal profile was determined. Men with oligospermia have heterogenous clinical profiles, and may require different therapeutic approaches.

Although estrogens in excess suppress spermatogenesis, physiological levels of estrogens (or the androgens/estrogens ratio) are required for the control of spermatogenesis (Carreau 2000) Conversion of androgens to estrogens is also required in order to ensure the integrity of the gonadotropin feedback mechanism in men, which is also essential for normal spermatogenesis (Rochira et al., 2001). Furthermore, low concentrations of 17 β -estradiol effectively inhibit male germ cell apoptosis, and dihydrotestosterone is also capable of inhibiting testicular apoptosis, but at much higher concentrations (Pentikainen et al., 2000). These reports support our concept of 'low dose estrogen-testosterone combination therapy for oligospermia'.

In conclusion, oligospermia with small testes and elevated serum FSH is considered a condition for which no proper treatment is available (Abyholm, 1983). Low dose estrogen-testosterone combination therapy may be such a treatment. This report further emphasizes the role that this therapy can play in the treatment of oligospermia in men presenting with different types of male infertility. Furthermore, it may represent a lower cost alternative to the assisted reproduction techniques that are usually applied in these conditions.

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