

Sperm Count Improvement in a Cancer-Surviving Patient

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Key Words

Aromatase inhibitors · Testosterone · Gonadotropins · Oligospermia · Oncological diseases

Abstract

Objective: To describe the case of a cancer-surviving patient who was treated with an aromatase inhibitor for fertility reasons with successful results. **Clinical Case:** A 30-year-old patient from our institute who had been submitted to bone marrow transplantation in the past as part of treatment for Hodgkin's disease had revealed oligospermia several times. His sperm count mean value was 33,500 cells/ml. He was treated with an aromatase inhibitor (letrozole, 2 mg/day) for 8 months. After this period, his sperm count had increased significantly to 1,000,000 cells/ml. **Conclusion:** A large number of cancer survivors express a wish for having babies. After their cure, a lot of them have a low count of spermatozooids, and we think that our results show an easy way of helping them.

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Introduction

Hypogonadism and oligospermic and azospermic conditions are common late effects of oncological treatments on the endocrine and reproductive systems. Following chemotherapy or radiotherapy treatment, a partial or total lack of spermatozoa as well as of Leydig and Sertoli cell function is frequently observed.

With the advent of new therapies, the survival period has been extended, and fewer relapses occur. Thus, we have a new population growing up who present with many problems not previously seen. Many oncological patients are treated during childhood, and very often sexual dysfunction and/or concerns about fertility occur only in adulthood. Sperm preservation is not often feasible, which leads to patients seeking treatment at an older age.

Treatment of male hypogonadism is easy and has been performed by providing patients with testosterone supplements. Fertility treatment using clomiphene or gonadotropin hor-

mones is more difficult and, in the latter case, expensive and painful. Nowadays, there is a new group of drugs – aromatase inhibitors – that can attain those objectives in an easier and more physiological manner. Some of these drugs have already been tested, and positive correlations were found between the duration of therapy in months and their strongest effects.

We describe the clinical case of an azoospermic cancer-surviving patient who was treated with letrozole, which led to an improvement in testosterone levels and a rise in sperm counts.

Clinical Case

A 30-year-old male patient suffering from Hodgkin's disease had undergone strong chemotherapy as preparation for bone marrow transplantation (BMT). He had survived, and after 3 years without receiving any therapy, his gonadal status was evaluated. He had no complaints and showed the following values: total testosterone (TT) – 419 ng/dl (400–900); free testosterone (FT) – 14.7 pg/ml (9–27); luteinizing hormone (LH) – 7.9 mIU/ml (<15); follicle-stimulating hormone (FSH) – 29.8 mIU/ml (<15), and estradiol (E₂) – 26.5 pg/ml (<11). Two spermograms were made in different weeks and revealed azoospermia.

Five and 7 years after BMT, he was tested again. The tests showed a slight increase in FSH and constant LH values. A sperm count revealed a slight improvement after 5 years, with a mean value (MV) of 100,000 cells/ml, but at 7 years it had decreased to an MV of 500 cells/ml (fig. 1). During year 7, the TT values remained more or less the same, but it was noted that the FT levels had decreased to 7.8 pg/ml (fig. 2).

The patient had no complaints regarding his sexual performance, but he expressed a strong wish to become a father. We decided to treat him with letrozole, and he took 2.5 mg/day over a period of 8 months (fig. 3). Tests of his androgen values and sperm cell counts were repeated at the end of that period.

Both LH and FSH had increased. LH increased to 48.7% (16.2 mIU/ml) and FSH to 26.3% (37.2 mIU/ml). E₂ decreased 71.3% (18.9 pg/ml); TT and FT showed a marked increase, doubling basal values with 110.6% (882.5 ng/dl) and 92.5% (28 ng/ml), respectively. As an indirect indicator of aromatase activity, T/E₂ was calculated. There was a rise of 193.75% (table 1; fig. 3, fig. 4, fig. 5). Sperm count improved to a MV of 1,000,000/ml (fig. 3; table 1).

Sampling Procedure and Hormone Assays

Blood samples for assays of serum TT, FT, E₂, LH and FSH were taken at 9 a.m. Serum TT, FT, FSH, LH and E₂ levels were assayed by chemiluminescence (Automated Chemiluminescence Systems; Bayer Corp., Diagnostic Division, Norwood, Mass., USA). The interassay coefficients of variation were 19.8, 5.6, 7.4 and 8.6%, respectively. Serum FT was measured by a solid-phase radioimmunoassay (Count-A-Count; Diagnostic Products, Los Angeles, Calif., USA). The interassay coefficient of variation was 10.4%.

For the sperm counts, samples were collected following 3 days of sexual abstinence on 2 different days. The concentration of spermatozoa was determined using the hemocytometer method after centrifugation (15 min) in accordance with WHO recommendations. All values were registered using a mean value of at least 2 determinants.

Discussion

Sperm concentrations can show marked variation even in the absence of medication or illness. However, the evolution of the variance in MV sperm counts in this patient receiving medication was very significant. Aromatase inhibitors have been used as a form of treatment by several authors. Very good results have been observed not only in patients but also in healthy elderly men.

Letrozole, a third-generation aromatase inhibitor, 2–5 times more potent than anastrozole, blocks the aromatization of androgens to estrogens in extragonadal sites, mostly in adipose tissue. Longcope and colleagues [1] induced a significant increase in TT with anastrozole in 37 elderly men who had basal values <350 ng/ml and decreased E₂ values.

In another study, T'Sjoen et al. [2] showed that an elevation of E₂ in elderly men is an explanation for lower TT levels. They compared an older with a younger group undergoing letrozole treatment and found a significantly higher reduction of E₂ in the older group. After 8 months of treatment, our patient also showed an elevation of TT and a decrease in E₂ levels.

In another study, Harden and MacLusky [3] noticed a normalization of serum TT levels and an improvement in sexual performance when prescribing letrozole to a 61-year-old man who suffered from seizures. A marked increase in gonadotropin was equally noted.

Believing that adipose tissue increases the conversion of TT to E₂ in obese men, Zumoff et al. [4] administered testolactone to that group. They registered a noticeable elevation of TT values.

Cohen [5] obtained similar results when, for the same reasons mentioned above, he used testolactone on obese hypogonadotropic hypogonadic men. Stephens and Polotsky [6] and Stokes et al. [7] found the same use for obese male subjects.

With the purpose of decreasing E₂ and not increasing prolactin values, Molitch and colleagues [8] gave anastrozole to a patient suffering from sexual dysfunction and prolactinoma. Under TT elevation, he improved his sexual performance and his prolactin levels did not show any elevation.

Improvements in sperm counts have equally been noted by other authors. Raman and Schlegel [9] obtained very good results in subfertile men who were subject to anastrozole and testolactone treatments, as did Gudeloglu et al. [10] and Jung and Seo [11].

We are convinced that the FSH elevation observed in our patient is the key to germinal improvement. It is well known that endogenous testosterone induced by LH elevation has a paracrine effect on Sertoli cells and thus can improve sperm secretion. Treatment involving testosterone management has an anticonceptive effect, because it has a negative impact on FSH levels; therefore, it should not be used for treating partially hypogonadic patients who desire to become a father.

This paper shows the utility of aromatase inhibitors. We believe that this therapeutic option is highly successful in the treatment of oligospermic and hypogonadic oligospermic patients with low/normal gonadotropin levels. It is an easy and painless form of therapy, as opposed to treatment with gonadotropin injections. With one single drug we can obtain two stimulation lines. It is also cheaper and free of major adverse effects.

Further prospective studies are obviously needed to improve our understanding and therapy management. We need to augment our experience, but we hope that we will obtain similar results in other cases and give our surviving patients hope and a better quality of life.

Statement of Ethics

The authors have no ethical conflicts to disclose.

Disclosure Statement

The authors have no conflicts of interest to declare.

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Table 1. Hormone values in basal conditions and after 8 months of letrozole treatment

	Before treatment	After 8 months of letrozole treatment	Variability, %
LH, IU/ml	7.9	16.2	+48.7
FSH, IU/ml	29.8	37.2	+26.3
E ₂ , pg/ml	26.5	18.9	-71.3
TT, ng/dl	419	882.5	+110.6
FT, pg/dl	14.7	28.3	+92.5
T/E ₂ ^a	0.16	0.47	+193.75
Cells/ml	33,500	1,000,000	

^a Divided by 100.

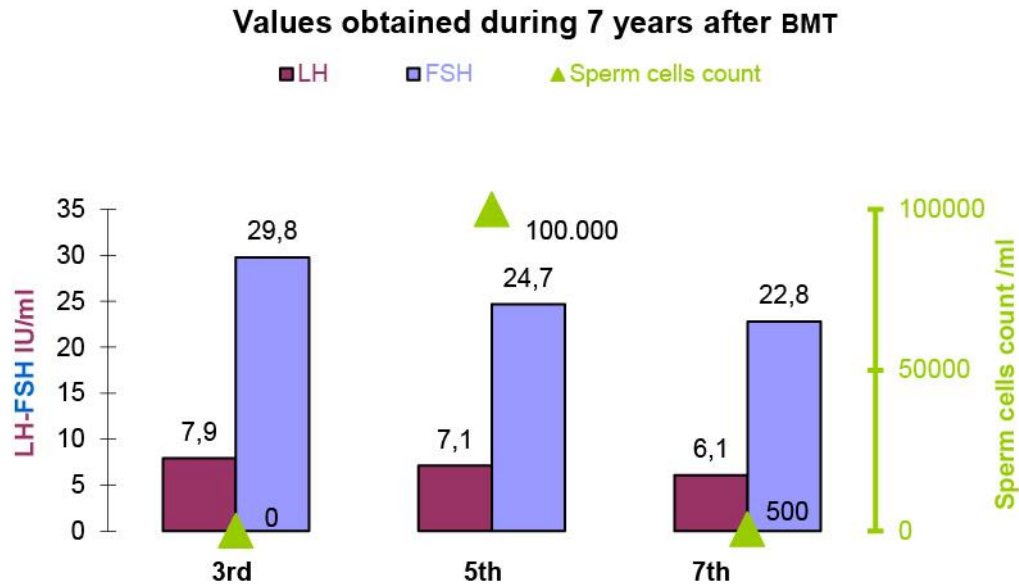


Fig. 1. Principal markers obtained after ‘cure’ of basal illness. MVs of gonadotropin and sperm cell counts obtained during the 3rd, 5th and 7th years.

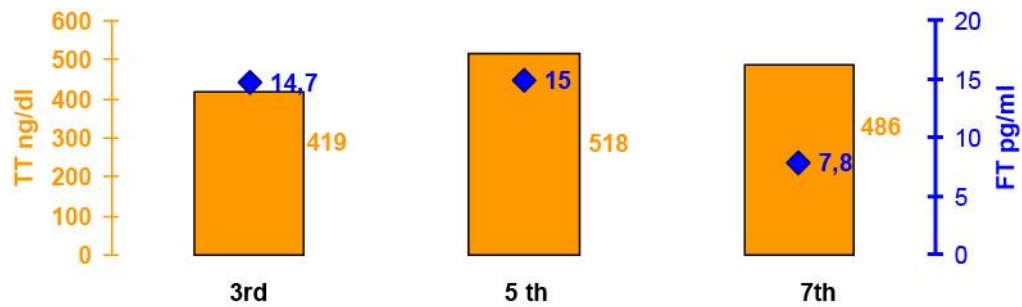


Fig. 2. TT and FT MVs obtained in the 3rd, 5th and 7th years after BMT.

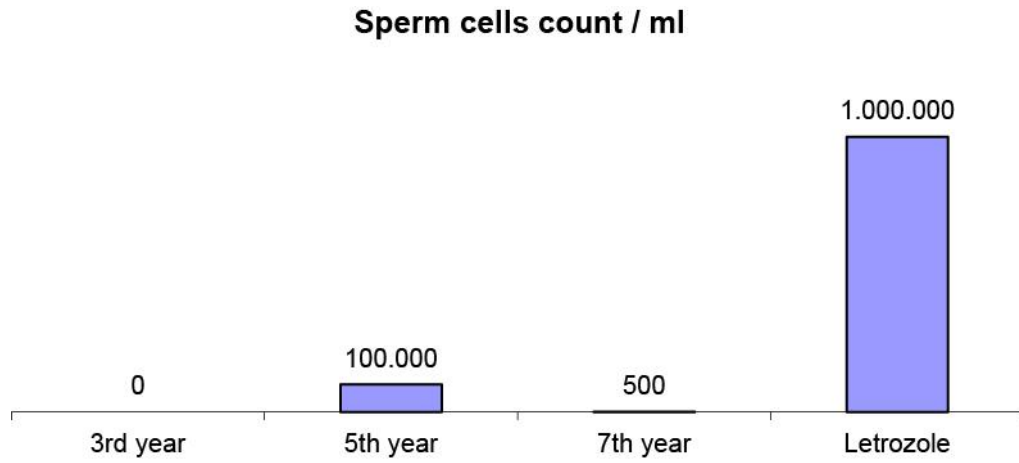


Fig. 3. Sperm cell count evolution along the 7 years after BMT and after letrozole treatment during 8 months.

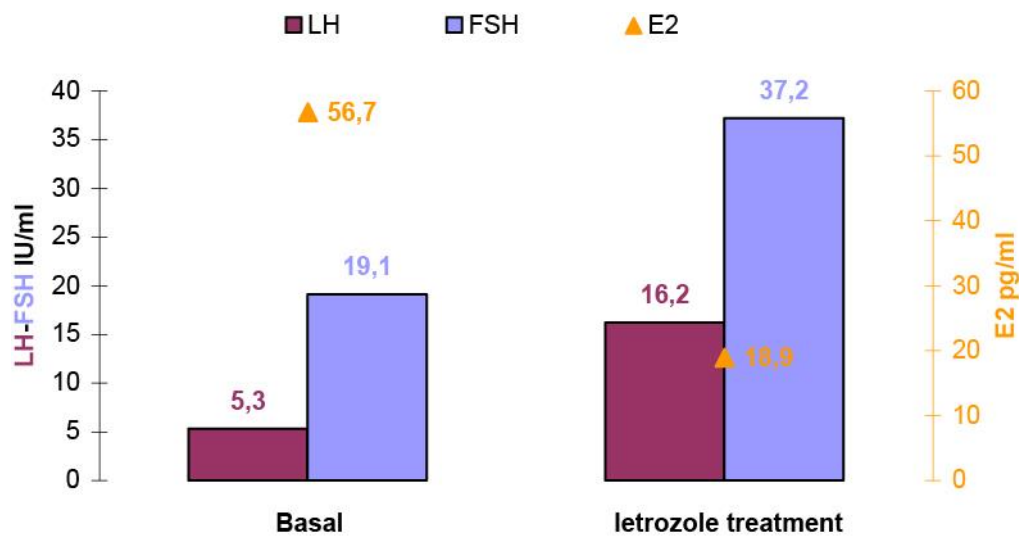


Fig. 4. Gonadotropin (LH/FSH) and E₂ MVs in basal conditions and with letrozole treatment.

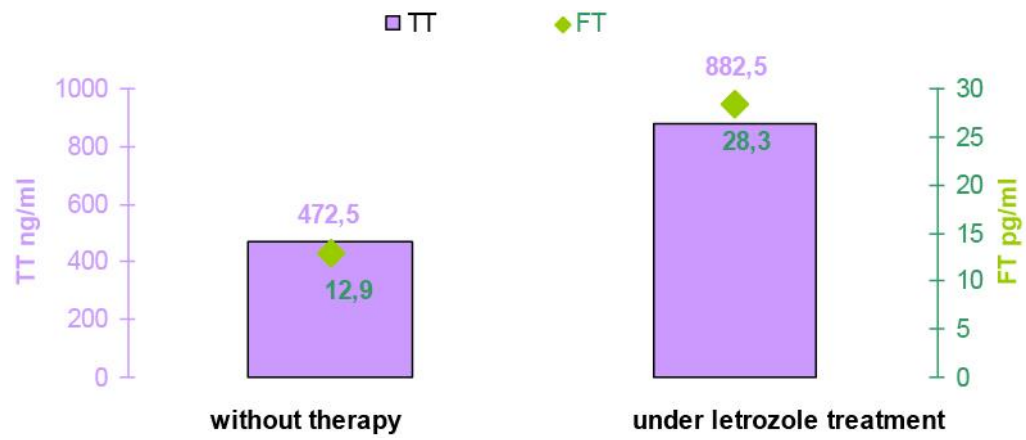


Fig. 5. MVs of TT and FT obtained in basal conditions and with letrozole treatment.