Case Reports and Reviews

Case Report

Effective Supplementation With Micronutrients in a Patient With Non-Obstructive Azoospermia and Varicocele: A Case Report

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Keywords

Azoospermia, Case Report, Varicocele, Male Infertility, Cyclofert Male™, Micronutrient Supplementation.

Abbreviations

ART: Assisted Reproduction Technology; FSH: Follicle Stimulating Hormone; IVF: In Vitro Fertilization; LH: Luteinizing Hormone; NOA: Non-Obstructive Azoospermia; OA: Obstructive Azoospermia; PCR: Polymerase Chain Reaction; RCT: Randomized Controlled Trial; TESA: Testicular Sperm Aspiration

Abstract

Background: *Non-obstructive azoospermia (NOA) is a form of male infertility, often associated with conditions influencing spermatogenesis, such as varicoceles. While varicocele repair is a standard intervention, the role of micronutrient supplementation in improving semen parameters and enhancing fertility outcomes in men with NOA and varicocele is promising.*

Case Summary: *The patient is a 30-year-old white Lebanese Caucasian male presenting with a previous diagnosis of NOA, with low testosterone levels and elevated follicle-stimulating hormone and luteinizing hormone levels. Clinical examination, hormonal assessment, scrotal ultrasound, and semen analysis revealed non-obstructive azoospermia associated with bilateral varicoceles. After ongoing bilateral varicocelectomy, the patient was prescribed Cyclofert Male™, a combination of L-carnitine L-tartrate, N-acetyl-cysteine, coenzymeq10, Zinc, folic acid, selenium, vitamin C, vitamin E, and Lycopene, at a dose of two tablets per day, for six months. At follow-up, semen analysis revealed improved sperm concentration; and successful in vitro fertilization (IVF) with blastocyst transfer was achieved.*

Conclusion: *This case reveals the potential role of micronutrient supplementation in improving semen parameters and IVF outcomes. Cyclofert Male™ offers a promising adjunctive and non-invasive treatment option for men with NOA and infertility.*

Introduction

The most severe form of male infertility is azoospermia, affecting nearly 1% of the male population and 10 to 15% of all men with infertility [1,2]. Azoospermia refers to the complete absence of spermatozoa in the ejaculate and is diagnosed by at least two semen analyses revealing no sperm in the semen. This condition could be caused by genital tract obstruction, called obstructive azoospermia (OA). In contrast, in 60% of the male population with azoospermia, nonobstructive azoospermia (NOA) is caused by impaired spermatogenesis or abnormalities in the function or structures of the testicles [3]. Diagnosis is generally based on patient history, physical examination, hormonal assessment, semen analysis, and genetic testing.

Most testicular causes of NOA are irreversible except varicoceles, which are abnormally dilated scrotal veins. Varicoceles are associated with excessive oxidative stress which adversely impacts spermatogenesis by increasing DNA fragmentation of sperm and leading to low sperm count and abnormal semen parameters. Varicocele management offers an opportunity for men with NOA to restore sperm count and achieve pregnancy either naturally or with assisted reproductive technology (ART) [4].

While varicocele repair is generally recommended for patients with clinically significant varicoceles [5] and is linked with improvements in almost all semen parameters [6], an increasing interest has emerged in the use of micronutrient therapy to improve fertility outcomes in men with azoospermia. Recent studies have shown that some micronutrients including zinc, selenium, folic acid, and antioxidants such as coenzyme Q10, L-carnitine, omega-3 fatty acids, and vitamins C and E have been linked to improved spermatogenesis and sperm quality [7–12], especially in varicocele cases by decreasing oxidative stress levels.

In this report, we present the case of a 30-year-old married male diagnosed with NOA and varicocele, and treated with bilateral varicocelectomy and supplementation with Cyclofert Male™, a fertility-enhancing combination of L-carnitine L-tartrate, N-acetyl-cysteine, coenzymeq10, Zinc, folic acid, selenium, vitamin C, vitamin E, and Lycopene.

Case presentation

Patient information

The patient is a 30-year-old white Lebanese Caucasian male, married for 3 years with no

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children, and working as an engineer. He presented to the French Hospital of the Levant in Lebanon, with a previous diagnosis of NOA, along with low testosterone levels and elevated follicle-stimulating hormone (FSH) and luteinizing hormone (LH) levels. A Y chromosome microdeletion test conducted before his admission yielded normal results. No history of systemic diseases, chemotherapy, radiotherapy, genitourinary tract infections, or scrotal traumas and surgeries were reported.

Physical examination

The physical exam assessed the testicular size, texture, and consistency, in a warm room. Mild testicular hypotrophy was observed, and grade 3 bilateral varicoceles were both visible and palpable based on the criteria of Dubin and Amelar [13].

Diagnostic assessment

A scrotal Doppler ultrasound was performed to confirm the physical exam findings. Based on Sarteschi's criteria for grading varicocele [14], it revealed bilateral grade III and IV varicoceles and was not suggestive of any signs of obstruction.

Semen analysis was performed according to the World Health Organization's recommendations (World Health Organization, 2021). The volume of the semen sample was 1.8 mL (>1.5 mL) and no spermatozoa were found in the sediment of the centrifuged sample, indicating azoospermia. Blood tests showed elevated serum levels of FSH at 17.16 mIU/mL (>7.6 mIU/mL) and LH at 10.1 mIU/mL (>8 mIU/mL), as well as low total testosterone level of 224 ng/dL (<300 ng/dL) [2].

The absence of obstructive pathology, small-sized testes, elevated gonadotropins, and low testosterone suggest spermatogenic failure which is indicative of NOA. Therefore, genetic analysis was investigated. The patient was screened for Y chromosome microdeletions by polymerase chain reaction (PCR) using a set of Y chromosome-specific sequence-tagged sites, with DNA concentration at 48.5ng/µL. The analysis revealed no complete or partial deletions.

Interventions

After the diagnosis of NOA and varicoceles, the patient underwent a bilateral varicocelectomy using the open inguinal (Ivanissevich) procedure and was prescribed Cyclofert Male™, twice daily for six months. Cyclofert Male™ is a fertility-enhancing supplement for men containing zinc, L-carnitine, vitamin C, vitamin E, lycopene, N-acetylcysteine, coenzyme Q10, selenium, and folic acid.

Follow-up and outcomes

Follow-up semen analysis 6 months post-supplementation revealed an improved sperm concentration of 4 million/ml. Even with a low sperm count post-treatment, in vitro fertilization (IVF) was pursued. Sperm retrieval was successfully carried out using testicular sperm aspiration (TESA) and resulted in the fertilization of 6 eggs. The embryos were then cultured to the blastocyst stage and frozen for future use. The patient is currently awaiting intrauterine insemination.

Discussion

This case report presents an approach for treating NOA and varicocele combining surgical and nutritional interventions. Cyclofert Male™ supplementation has been shown to have positive effects on sperm parameters, observed after 6 months of supplementation.

Our observation in terms of sperm concentration improvement aligns with previous findings showing that supplementation with Cyclofert Male™ for 3 months increased sperm count by 64% in males with infertility compared to untreated men [16]. Another study excluding OA and NOA cases, showed similar improvements in semen parameters including sperm concentration, after 3 and 6 months of Cyclofert Male™ supplementation [17]. This further highlights the efficacy of Cyclofert Male™ as a supportive therapy for enhancing sperm quality and concentration in infertile men, potentially complementing other therapeutic interventions for NOA associated with varicocele.

The association between varicocelectomy and improvements in semen parameters remains inconsistent, although the majority of studies acknowledged the positive effects that can varicocelectomy have on semen quality [18,19]. The largest and most recent meta-analysis on varicocele patients demonstrated significant improvements in all semen parameters, including sperm concentration, following varicocele repair in infertile patients with clinical varicocele [6]. Additionally, according to studies, these improvements generally occur within the first 3 months following varicocele repair [18,20]. In this case, despite the improved sperm concentration and the successful fertilization, separating the effects of Cyclofert Male™ from the effects of varicocelectomy seems challenging without a randomized controlled trial (RCT). A follow-up at 3 months post-varicocelectomy with semen parameters compared at both 3 and 6 months would have provided a better understanding of whether the improvement in sperm concentration and quality beyond the 3 months post-varicocelectomy could be attributed to Cyclofert Male™ supplementation.

While our patient had slightly improved sperm concentration at 6 months, the result remained below the normal and acceptable range (>15 million/mL) [21] for achieving natural conception or successful intrauterine insemination. Therefore, in this case, we opted to proceed directly to IVF [21,22]. Time is a key factor influencing sperm quality improvement after varicocelectomy, and the most substantial improvements generally occur within the first 3 months following varicocele repair [18]. In this case, the successful fertilization and blastocyst formation in IVF treatment reflect improved sperm quality and suggest that the addition of Cyclofert Male™ to the patient's treatment strategy may have supported and prolonged the benefits of varicocelectomy by reducing oxidative damage and improving spermatogenesis beyond 3 months. The strength of this approach lies in highlighting the positive impact of combined therapy in patients with NOA and varicocele, by optimizing fertility outcomes.

This case informs clinical practice by highlighting the role of considering micronutrient supplementation as part of the treatment plan, particularly for men with NOA associated with varicocele. Incorporating supplements like Cyclofert Male™ as adjunctive therapy can help optimize spermatogenesis and improve fertilization rate, offering men a viable and cost-effective infertility care strategy. Future high-quality RCTs with large sample sizes are needed to confirm the impact of Cyclofert Male™ in reducing oxidative stress and improving the quality of spermatozoa, and to establish evidence-based guidelines for its use in male infertility treatment.

Conclusion

This case report highlights the potential impact of micronutrient supplementation in treating NOA associated with varicocele. Cyclofert Male™ showed promising results in

improving sperm concentration and fertility outcomes following varicocelectomy. The observed improvements support the evidence that certain micronutrients and antioxidants may effectively enhance spermatogenesis, offering an adjunctive and non-invasive treatment option for men with NOA and infertility.

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