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Case Report

Erythrocytosis Secondary to Testosterone Therapy in a Male with Cryptorchidism: A Case Report☆,☆☆

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SUMMARY

Hypogonadism is association with aging (andropause) can now be recognized earlier and treated with testosterone, thus resulting in the relief of symptoms and better quality of life. However, any patients that are treated with testosterone must be closely monitored in order to avoid the development of sleep apnea, cardiovascular diseases, hepatic dysfunction, plasma lipid disorders, or erythrocytosis, all of which are potential side effects of treatment. Herein, we present a case of erythrocytosis secondary to testosterone treatment in a patient with cryptorchidism. Hemoglobin levels returned to normal soon after phlebotomy and discontinuation of testosterone therapy. Physicians should be aware of the side effects of testosterone replacement therapy and cautiously monitor patients in order to avoid these side effects and cumbersome and expensive laboratory tests.

1. Introduction

Testosterone is routinely implemented as replacement therapy to treat cases of hypogonadism. Hypogonadism is characterized by low testosterone levels in association with diminished libido, sexual dysfunction, depression, malaise, reductions in bone density and muscle mass, and anemia. Hypogonadism in association with aging (andropause) is can now be recognized earlier and treated with testosterone, thus resulting in the relief of symptoms and better quality of life. However, it is necessary that patients who are treated with testosterone be closely monitored in order to avoid the development of sleep apnea, cardiovascular diseases, hepatic dysfunction, plasma lipid disorders, and erythrocytosis, all which are potential side effects of treatment[1–3]. Herein, we present a case of erythrocytosis secondary to testosterone treatment in a patient with cryptorchidism.

2. Case report

A 77-year-old man was admitted to a secondary care hospital due to severe dizziness and headaches. His laboratory findings included 62% hematocrit (Hct), 18.3 g/dL hemoglobin (Hb), 8200 white blood cells/μL (54% neutrophils), 138,000 platelets/μL, and an erythrocyte sedimentation rate of 10 mm. The patient was diagnosed with erythrocytosis and underwent venesection in order to obtain one unit of blood. He was referred to our hospital for further workup and treatment. The patient was clinically assessed using computed tomography (CT) scans of the brain, abdomen, and chest in order to exclude ischemic stroke and paraneoplastic erythrocytosis, respectively. The CT scans appeared normal except for findings that suggested a previous tuberculosis infection in chest. The red blood cell mass was considered higher than normal, while the erythropoietin (EPO) level was normal. No *in vitro* endogenous autonomous erythroid colonies were grown from patient's bone marrow cultures. We also checked for the JAK2V617F mutation, which is positive in 95% of patients with polycythemia vera[4], but patient was negative. Arterial blood gas levels were normal and there were no signs or symptoms of chronic cardiac or pulmonary diseases. The patient was a nonsmoker who lives at sea level. His occupation does require contact with carbon monoxide. A detailed personal medical history revealed that apart from having been diagnosed with a thrombotic stroke 2 years prior, the patient had been parenterally receiving 250 mg testosterone enanthate every 3 weeks for approximately 18 years after undergoing an operation for cryptorchidism.

The patient had been instructed by his doctor to perform follow-up laboratory tests after starting testosterone therapy, including hemoglobin-hematocrit analysis on an annual basis. His hematocrit

☆ The privacy of the patient has been maintained and anything that might allow his identification has been obscured.
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had varied between 53–54% for the last 4 years, but no special work up was considered necessary.

Testosterone treatment was immediately interrupted following the diagnosis of secondary erythrocytosis. On a follow-up visit 2 months later, his hemoglobin and hematocrit values had returned to normal (15.3 Hb g/dL, 45.2% Hct).

3. Discussion

There is significant controversy regarding the use of testosterone replacement therapy (TRT) in aging men due to the lack of large-scale, long-term studies to assess the potential risks and benefits. However, there are reports that suggest that TRT might be associated with a wide range of benefits for men with hypogonadism[1].

In our case, the patient had been parenterally receiving 250 mg testosterone enanthate every 3 weeks for approximately 18 years after undergoing an operation for cryptorchidism; however, no special analyses had been performed in recent years.

Cryptorchidism is among the most common genital problems encountered in pediatrics. This condition refers to an undescended or maldescended testicle and appears to be a cause of primary hypogonadism. In the vast majority of cases, the disease is congenital and is associated with testicular cancer and infertility. The treatments of choice include orchiopexy and hormonal therapy, mainly via the administration of gonadotropin-releasing hormone (GnRH analogues) and human chorionic gonadotropin in order to topically maintain adequate levels of testosterone[5]. Our patient did already knew that he had cryptorchidism. However, he initially objected to receiving treatment until he was made aware of the potential link between untreated cryptorchidism and an increased incidence of cancer.

Erythrocytosis is the most frequent side effect of testosterone treatment, especially in older men. The injection is associated with a higher potential for erythrocytosis than topical preparations, especially at supraphysiologic doses. An increase of up to 44% from baseline hematocrit has been reported[6–8]. Hematocrit and hemoglobin increase in a linear, dose-dependent manner. Although this might be beneficial to older patients with anemia, the long-term health consequences of erythrocytosis are unknown. In epidemiological studies, high hematocrit levels are associated with an increased risk of cerebrovascular disease and mortality[7].

The exact mechanism responsible for the stimulatory effect of testosterone in erythropoiesis is not fully understood. Recent findings suggest that it might be mediated by factors other than EPO or soluble transferrin receptors[3]. Testosterone might also directly affect bone marrow hematopoietic stem cells. Previous reports have shown that androgens promote the differentiation of erythroid colony-forming units into erythropoietin-responsive cells. Furthermore, hemoglobin synthesis is enhanced via increases in intestinal iron absorption and the incorporation of iron into red blood cells following testosterone treatment. Finally, erythrocytes live longer due to higher levels of 2,3-diphosphoglycate after androgen use.

In conclusion, TRT is indicated for treating cases of classical hypogonadism. However, the use of TRT in older men with mild hypogonadism due to partial androgen deficiency should be carefully weighed by the consulting physician after considering the potential risks and benefits. In our case, it was considered necessary, but the hematocrit and hemoglobin levels of the patient should be monitored on a regular basis after 0, 3, 6, 12, and 18 months of therapy and annually thereafter, as well as after every dose modification or after the use of any intervention, such as phlebotomy or the discontinuation of testosterone therapy, in order to prevent erythrocytosis[1]. Thus, the risk of cerebrovascular disease that accompanies erythrocytosis will be significantly reduced, and patients will not be subjected to unnecessary and expensive laboratory exams. Unfortunately, testosterone levels were not monitored in our patient. Upon admission, his total testosterone serum level was 755 ng/mL (normal range: 212–742 ng/mL) because he had received a testosterone injection 3 weeks prior. After the discontinuation of treatment, the patient's hemoglobin levels returned to normal. The consulting endocrinologist is currently considering restarting treatment at a lower dose of testosterone and advocates closely monitoring this patient in order to prevent potential side effects.

This case highlights the need to closely monitor patients who are receiving TRT. This is often ignored by both patients and treating physicians, and may result in detrimental side effects.

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