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Case Report

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Polycythemia with Low Erythropoietin Level after Testosterone Supplementation

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Abstract

The pathogenesis of testosterone-induced polycythemia is thought to be mediated via increased production of erythropoietin. Here we describe a patient who presented with polycythemia due to testosterone supplementation. However, erythropoietic serum level was low. Following the cessation of testosterone supplementation, hemoglobin and erythropoietin levels returned to normal. This suggests that erythropoietin may be dispensable for testosterone-induced polycythemia.

Keywords: Erythropoietin; Testosterone; Erythrocytosis; Polycythemia.

Introduction

Testosterone-induced polycythemia is thought to be, at least in part, due to the testosterone-induced hyper production of erythropoietin (EPO) [1]. Here, we present a case of testosterone-induced polycythemia with a low serum EPO level, suggesting that EPO is dispensable for testosterone-caused polycythemia.

Case Report

A 34-year-old previously healthy male presented as a potential allogeneic hematopoietic cell transplant donor. Routine donor eligibility tests revealed elevated hemoglobin (206 g/L) and hematocrit (0.58). He was clinically euvolemic. He reported self-administration of testosterone enanthate, 150 mg IM weekly, for bodybuilding. Investigations were remarkable for low EPO serum level (3.5 U/L, reference range 4.0-20.0) and elevated carboxyhemoglobin (11.1%, reference range ≤3.0%) attributed to smoking. JAK2 gene was not mutated. Creatinine plasma level was normal (89 umol/L, reference range 50-120). Within 5 months of cessation of testosterone, the patient's hemoglobin, hematocrit, and EPO level returned to normal (Table 1).Carboxyhemoglobin remained high at 10.9%, consistent with continued smoking.

Parameter	Reference Range	May 7, 2018	Nov 12, 2021	Nov 15, 2021	Nov 24, 2021	Jan 12, 2022	Mar 9, 2022
Hemoglobin	137–180 g/L	170	206	205	192	180	169
Serum EPO	4.0–20.0 U/L	-	3.5	-	-	7.4	13.3
Comment		Off testosterone	End of a 4-mo course of testosterone	Off testosterone			

Table 1: Hemoglobin and testosterone levels at baseline, immediately after a 4-month course of testosterone, and days to months after the testosterone discontinuation.

Discussion

Elevations in testosterone can lead to polycythemia through multiple mechanisms, including stimulation of the estrogen receptor alpha (ERa), the stimulation of EPO, suppression of hepcidin, and bone marrow stimulation by increasing dihydrotestosterone [2-5]. Among these, the EPO-mediated mechanism has been thought to be important [1].

EPO is produced in the kidney in response to hypoxia and is released to act on erythrocyte progenitors, especially at the Colony Forming Unit-Erythroid (CFU-E) stage, as a survival, proliferation, and differentiation factor. The concept of a modified EPO 'set point' has been introduced, with testosterone raising the normal homeostatic EPO level, perhaps through hepcidin suppression, leading to increased erythropoiesis and a failure of negative feedback inhibition on EPO [1,6]. However, subsequent investigations have not consistently replicated these findings, with trials showing no difference in EPO levels between testosterone-supplemented men and those receiving placebo, despite the anticipated changes in hemoglobin [7,8]. In the patient we describe, EPO levels were low at the presentation of polycythemia and returned to normal following testosterone cessation, with subsequent hemoglobin drop. Thus, feedback mechanisms were properly acting to reduce EPO in the presence of testosterone-driven polycythemia.

EPO is also stimulated by oxygen demand and thus is elevated with hypoxia [9]. Given the patient's high carboxyhemoglobin levels attributed to smoking, we would expect EPO to be elevated to stimulate red blood cell production. Given the observed low EPO level despite the elevated carboxyhemoglobin, this further suggests that in our patient the testosterone-induced polycythemia was not driven via testosterone-induced EPO overproduction.

In conclusion, we describe a case of testosterone supplementation-induced polycythemia with reduced EPO that increased after testosterone cessation. It has been controversial whether EPO is dispensable for testosterone-induced polycythemia [1,8]. Thus, this case report is important as it suggests that for the induction of polycythemia by testosterone, EPO is dispensable.

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Conflicts of Interest: The authors declare no conflict of interest.

References

1. Bachman E, Travison T.G, Basaria S, Davda M.N, Guo W, et al (2014). Testosterone Induces Erythrocytosis via Increased Erythropoietin and Suppressed Hepcidin: Evidence for a New Erythropoietin/Hemoglobin Set Point. J. Gerontol. A. Biol. Sci. Med. Sci. 69: 725–735.
2. Ohlander S.J, Varghese B, and Pastuszak A.W. (2018) Erythrocytosis Following Testosterone Therapy. Sex. Med. Rev. 6: 77–85.
3. Shahidi N.T. (1973). Androgens and Erythropoiesis. N. Engl. J. Med. 289: 72–80.
4. Guo W, Bachman E, Li M, Roy C.N, Blusztajn J, et al. (2013) Testosterone administration inhibits hepcidin transcription and is associated with increased iron incorporation into red blood cells. Aging Cell. 12: 280–291.
5. Aghazadeh M, Pastuszak A.W, Johnson W.G, McIntyre M.G, Hsieh T.M, et al (2015) Elevated Dihy-drotestosterone is Associated with Testosterone Induced Erythrocytosis. J. Urol. 194: 160–165.
6. Bachman E, Feng R, Travison T, Li M, Olbina G, et al. (2010). Testosterone Suppresses Hepcidin in Men: A Potential Mechanism for Testosterone-Induced Erythrocytosis. J. Clin. Endo-crinol. Metab. 95: 4743–4747.
7. Hennigar S.R, Berryman C.E, Harris M.N, Karl J.P, Lieberman H.R, et al (2020). Testosterone Administration During Energy Deficit Suppresses Hepcidin and Increases Iron Availability for Eryth-ropoiesis. J. Clin. Endocrinol. Metab. 105: e1316–e1321.
8. Maggio M, Snyder P.J, Ceda G.P, Milaneschi Y, Luci M, et al. (2013). Is the haematopoietic effect of testosterone mediated by erythropoietin? The results of a clinical trial in older men. Andrology 1: 24–28.
9. Haase V.H. (2013). Regulation of erythropoiesis by hypoxia-inducible factors. Blood Rev. 27: 41–53.