

Clinical Case Seminar

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Dry cough after testosterone undecanoate injection: a case report.

Roberto Vita¹, Giovanni Capodicasa¹, Sarah Perelli¹, Salvatore Benvenga^{1,2,3}

¹ Department of Clinical and Experimental Medicine, University of Messina, Messina, Italy

² Master Program on Childhood, Adolescent and Women's Endocrine Health, University of Messina, Messina, Italy

³ Interdepartmental Program of Molecular & Clinical Endocrinology and Women's Endocrine Health, University hospital, A.O.U. Policlinico G. Martino, Messina, Italy.

Abstract

Testosterone esters are administered in oil vehicle via the intramuscular route. Rarely, dry cough together with faintness, diaphoresis, anxiety and syncope caused by pulmonary oil microembolism(POME) may occur. POME events are generally self-limited and last a few minutes. Very rarely they need oxygen therapy. Pathophysiology is still unclear. Here we report a case of POME occurring shortly after injection of testosterone undecanoate. The patient, a transmen on cross-gender hormonal treatment, was worried for the possible withdrawal of testosterone therapy. We reassured him and explained that he could continue his treatment provided that testosterone injections should be kept properly administered.

Key-Words: testosterone; cough; pulmonary oil microembolism; gender dysphoria

Introducing Member : Roberto Vita

Corresponding Author: Roberto Vita - rvita@unime.it

Introduction

Testosterone therapy is used as either replacement in hypogonadal male [1], or to affirm the desired sex in female subjects with gender dysphoria(transmen) [2]. Testosterone esters are administered almost exclusively in oil vehicle via the intramuscular route [1]. Particularly, castor oil is used to increase solubility of these lipophilic compounds and to impart a sustained pharmacokinetic absorption profile. Intramuscular testosterone is well tolerated, one of the most adverse effects being local irritation [3]. We report here a case of paroxysmal cough triggered by intramuscular testosterone injection, an uncommon adverse effect reported shortly after depot oil injections of steroids.

Case Report

A transmen started intramuscular testosterone enanthate at the age of 26 years, and at 28 he underwent bilateral mastectomy, hysterectomy and bilateral annessiectomy. He attended regularly

our outpatients clinic twice per year from the age of 26. Six months before our last observation he has been switched from testosterone enanthate to testosterone undecanoate every 3 months. His testosterone levels had been stably in the mid range of normality for men (400-500 ng/dl) without any adverse effect. Also, hematocrit had been always kept <48%. He took advantage of his brother-in-law, an experienced nurse, for the regular testosterone injection. During the last visit, he revealed that a few minutes after the last testosterone injection (i.e. the third injection of testosterone undecanoate), he suddenly experienced, for the first time ever, urge to cough together with dizziness, sweating and mild chest pain. Although these symptoms lasted about 5 minutes, faintness continued for a few hours. At visit, the patient was worried and asked if he should have discontinued hormonal treatment for his safety, with subsequent loss of androgenization.

Discussion.

Pulmonary oil microembolism (POME) is a rare adverse effect during steroid injections [1]. Particularly, the frequency of POME is 15-20 cases per 1,000 injection of testosterone undecanoate, and it is somewhat higher compared with testosterone enanthate, probably because the injected oil volume is greater in case of testosterone undecanoate (4 vs. 1 ml) [4].

Symptoms of POME include dry cough, not caused by concomitant asthma or airways infections, together with faintness, diaphoresis, anxiety and syncope. These symptoms may overlap with those of anaphylaxis, which can occur after testosterone injection. Diagnosis is merely clinical, and generally, other examinations are not needed. POME typically occurs concomitantly or shortly after steroid injection, and in most cases symptoms abate within 60 minutes [3]. Patients may also report an unpleasant medicine taste in their mouth. Oxygen therapy is rarely needed. Very rarely, acute respiratory distress syndrome occurs [5].

Physiopathology of POME is still debated. The occasional recurrence supports a non-allergic basis, and rather, POME is considered a circumstantial, unpredictable adverse event. Entry of microscopic oil droplets into systemic circulation, and subsequently, through the right heart into pulmonary circulation, has been proposed [3,4]. Exhalation of a volatilized essence from the oil, capable to trigger cough receptors in the respiratory tract may explain why, not uncommonly, patients complain a medicinal or "oily" taste [3]. However, genetically determined prothrombotic diathesis and other anatomic predisposing factors may be necessary, as POME may recur over time [4]. Inadvertent intravenous administration can be prevented by aspiration after puncture. Pharmaceutical companies recommend also injecting the preparation slowly (for ≥ 2 minutes) and deeply into the gluteal muscle (upper outer quadrant of the buttock). However, a number of POME events, such as the one here reported, have occurred even after cautious and careful

injection technique. Lymphatic channels uptake of oil droplets and subsequent venous access has been hypothesized [3].

POME prevalence ranges from 1% to 2% [6,7]. The risk of POME is seemingly not influenced by age and purpose of treatment (i.e. replacement or cross-gender therapy). In a recent Australian study, the authors reported 56 POME episodes after 3022 injections (2%) of testosterone undecanoate in 347 patients. Nine of the 43 patients who experienced POME were transmen, and none required oxygen therapy [4].

Concerning the case here reported, we reassured the patient saying that there was no need to discontinue testosterone, renewing the importance of a proper administration of this drug.

In conclusion, POME is a rare adverse effect in patients on intramuscular testosterone. POME is generally transient, and does not require medical intervention. Nevertheless, it has to be kept in mind that it may recur over time.

Conflicts of Interest: There is no potential conflict of interest, and the authors have nothing to disclose. This work was not supported by any grant.

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