AMI and Anabolic-Androgenic Steroids: Case Report with Systematic Review

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Abstract: Introduction: Coronary artery disease (CAD) represents approximately 390 thousand deaths per year in Brazil and is associated, among other predictors, with the use of anabolic and androgenic steroids (AAS).

Objective: To analyze a clinical case of a patient who suffered AMI after abuse of AAS. A systematic literature review has been carried out to physiologically analyze the main factors that can lead to AMI with the use of these hormones.

Methods: The EVR patient, 41 years old, denies any comorbidities or use of medications. He has been admitted to the emergency room due to typical angina-precordial pain in tightness associated with eventual back pain and paresthesia of both upper limbs, after intense physical effort at the gym, without improvement at rest, and with partial improvement after first care at the health unit. The patient was hypertensive in an emergency bed after the occurrence of ST elevation. The patient alleges the use of anabolic steroids for one month. The patient presented with obstructive atherosclerotic coronary artery disease with total occlusion of the anterior descending artery.

Systematic review: A total of 89 clinical studies have been compared and submitted to eligibility analysis, with 50 studies selected, according to the PRISMA rules.

Results: Long-term consumption of AAS may cause pathological changes, however, AAS can increase protein synthesis, muscle growth, and erythropoiesis.

Conclusion: Abuse of AAS has a toxic cardiovascular effect, which significantly increases the incidence of cardiovascular diseases.

Keywords: Anabolic-androgenic steroids, cardiovascular disease, atherosclerosis, angioplasty, acute myocardial infarction, EVR.

1. INTRODUCTION

In 2017, according to information from the World Health Organization (WHO), the incidence of Coronary Artery Disease (CAD) was over ten million [1]. In Brazil, CAD is responsible for about 390 thousand deaths per year [2] and are associated with several predictors, including advanced use of Androgenic Anabolic Steroids (AAS), age, sex, smoking, obesity, hypertension, diabetes, genetic factors, hypercholesterolemia and sedentary lifestyle.

In this scenario, AAS is a family of hormones that exhibit anabolic and androgenic properties [3]. The lifetime prevalence of AAS among adolescent males in Western countries is 5% to 10% [4]. Scientific evidence shows that there is an association between the abuse or non-use of AAS with the increased risk of sudden cardiac death, acute myocardial infarction (AMI), abnormal lipid profile, and heart failure [5-7].

In this sense, cardiovascular responses to AAS occur due to certain myocardial receptors that have transcription regulatory functions, leading to cardiac hypertrophy [8-10]. Also, the effect of AAS can cause fibrosis and intimal hyperplasia of intramural coronary arteries, resulting in chronic ischemic damage and vasospasm in vascular endothelial cells [7, 11]. Besides, higher doses of AAS are also associated with increased platelet aggregation, producing a procoagulant state, through the dose-dependent prothrombotic profile [12, 13]. To corroborate this, an autopsy study carried out in Sweden, involving 34 male users of AAS, revealed chronic patholo-
gies, specifically left ventricular hypertrophy, fibrosis, and coronary artery disease [11]. Other studies also confirm these complications [14-18].

Despite this, steroid diversity, doses, and uncertain risks exist. Also, there is great uncertainty regarding the off-label use of AAS abuse time. In this sense, the literature demonstrates a fairly consistent level of clinical severity and pathological consequence among patients who abuse AAS between 18 and 50 years, both for a period of less than 1 year and up to 20 years [4, 15, 19-22].

In this context of the manifestation of CAD and the consequent AMI with an elevation of the ST segment due to the use of AAS, primary percutaneous coronary intervention is the most important reperfusion strategy [23-25]. However, its accomplishment within the defined deadlines is a great challenge [26]. Therefore, the diagnosis of CAD is based on the association of clinical history and complementary exams [27-29].

Therefore, the present study aimed to analyze a report of a patient who suffered AMI after abusive use of AAS followed by a systematic review of the literature to scientifically support what happened, as well as to point out physiologically the main factors that lead to infarction with the use of these hormones.

2. METHODS

2.1. Case Report

The EVR patient, 41 years old, denies any comorbidities or use of medications. He has been admitted to the emergency room due to typical angina-precordial pain in tightness associated with sporadic back pain and paresthesia of both upper limbs, after intense physical effort at the gym, without improvement at rest, and with partial improvement after first care at the health unit. The patient was hypertensive in an emergency bed, after the occurrence of ST-elevation AMI, an electrocardiogram was performed (Fig. 1). He has medicated with Isordil, AAS, and morphine. He was hemodynamically stable, eupneic in O₂ catheter, Blood pressure: 174/74, HR: 88, and Fr: 20. He denied syncope or other changes. Nonspecific chest pain for four days during physical activity that stopped at rest. The patient alleges the use of anabolic steroids for one month (Testorena and Decadurabolin, one ampoule IM on alternate days for one month before acute myocardial infarction), in addition to protein and vitamin supplements, and training with greater effort load for six months. She denies comorbidities and regular medical follow-up. In family history, the father infarcted at 65 and maternal CAD in addition to dyslipidemia. After examination of catheterization, the patient presented with obstructive atherosclerotic coronary artery disease with total occlusion of the anterior descending artery. During catheterization, ventricular tachycardia has been observed, which has reversed after 300 mg intravenous bolus amiodarone. The patient has referred for catheterization and underwent angioplasty with a stent in the left radial descending artery (Figs. 2 and 3), being successful with this procedure.
2.2. Settings

The study took place in the Department of Hemodynamics and Interventional Cardiology, Beneficência Portuguesa Hospital and Domingo Braile Institute of São José do Rio Preto, São Paulo, Brazil. All data were strictly kept confidential.

2.3. Study Design

The present study was a Case Report followed by the Systematic Review on the importance of catheterization and angioplasty procedures to resolve arterial occlusions. For the development of the case report, the rules of the CARE case report (https://www.care-statement.org/) have followed. The predictors were Anabolic-androgenic steroids, Cardiovascular disease, Atherosclerosis and Angioplasty Acute myocardial infarction. After literary search criteria using the MeSH Terms that were cited in the item below on “Search strategies”, a total of 89 clinical studies were compared and submitted to the eligibility analysis and, after that, 50 studies were selected, following the systematic review rules - PRISMA (Transparent reporting of systematic reviews and meta-analysis-https://www.prisma-statement.org/).

2.4. Data Sources and Search Strategy

PUBMED, EMBASE, OVID and COCHRANE LIBRARY databases have searched for analysis of the “risk of using anabolic steroids in occlusion of arteries” in the literature. A combination of the keywords with AND and the Boolean operator “NOT” was used. The title and abstracts have been examined in all conditions.

2.5. Study Selection and Risk of Bias in Each Study

Two independent reviewers (1 and 2) performed research and study selection. The data extraction was performed by reviewer 1 and fully reviewed by reviewer 2. A third investigator decided on some conflicting points and made the final decision to choose the articles. Only studies reported in Portuguese and English have been evaluated. The COCHRANE instrument was adopted to assess the quality of the included studies.

2.6. Risk of Bias

Considering the Cochrane tool for risk of bias, the overall evaluation resulted in six studies with a high risk of bias and four studies with uncertain risk. The domains that presented the highest risk of bias have related to some patients and risk factors with the use of AAS. Also, the absence of the source of financing in 4 studies. Further, three studies did not disclose the information on the conflict of interest statement.

3. RESULTS AND DISCUSSION

The present case report showed total occlusion of the left anterior descending artery in a male patient who made heavy use of anabolic steroids over thirty days. After percutaneous coronary intervention with stent implantation in the anterior descending artery, the patient progressed successfully. The work presented by Fahey et al., 2019, showed the same involvement in the artery in a female patient [30]. Another study also showed that acute thrombotic occlusion in the coronary arteries has an incidence of only 2.5%.

Also, an example of successful treatment with a stent due to thrombotic occlusion was with a 43-year-old woman who was hospitalized with severe chest pain, with an elevation of the ST segment [31]. In this context, the collateral flow to the territory of the infarction artery after AMI may be associated with better clinical results [32].

Thus, a randomized study of arterial occlusion showed long-term results in 2,173 patients with total artery occlusion from 3 to 28 days after AML. There were important differences in baseline clinical and angiographic characteristics. According to this study, the higher collateral grade has been related to a lower mortality rate, heart failure class III,
and IV, but it has not been associated with the risk of reinfarction. Therefore, in recent myocardial infarction, the occluded artery is correlated with the predictors of the main clinical outcomes such as death and reinfarction. Besides, delayed artery recovery, in addition to medical therapy, has no benefits compared to drug therapy alone. Therefore, the decision to revascularize patients with recent AMI should not be based on the presence or degree of angiographic collateral [33].

Despite this, the prognosis of chronic total occlusion in the coronary arteries in patients with AMI undergoing primary angioplasty remains controversial in the literature. Thus, a study analyzed the prognosis of chronic total occlusion in coronary arteries and the role of the left ventricular ejection fraction in this analysis. Prospective infarction patients with ST-segment elevation who underwent primary angioplasty have included. Chronic total occlusion was present in 125 of 1176 patients (10.6%). The median follow-up was 339 days, and 64 (5.8%) patients died in the first six months. Also, patients with chronic total occlusion had more comorbidities, worse ventricular function, and higher mortality. Chronic total occlusion did not behave as an independent predictor of mortality when the left ventricular ejection fraction has included in the analysis [34].

In this context, based on the use of AAS, a case report study showed a 30-year-old bodybuilder man with chest pain when resting, had no history of cardiovascular risk, and did not present changes in laboratory tests. However, the patient said that he had been using testosterone orally for several years, and this has been confirmed with features including loss of libido, erectile dysfunction, reduction in testicle size, and follicle suppressed by stimulating hormone and luteinizing hormone in pituitary function tests [35]. The electrocardiogram showed anteroposterior ST elevation. The patient underwent primary percutaneous coronary intervention (P-PCI). During PCL, a large thrombus was removed from the left anterior descending artery. There was no evidence of atherosclerotic disease. A stent was not implanted due to the risk of thrombus dissemination. Thus, higher levels of endogenous testosterone were associated with better cardiovascular outcomes in the elderly, but not in men < 70 years. However, the effect of the cardiovascular risk of exogenous high-dose exogenous testosterone in the long term is associated with the risk of thrombosis polycythemia [35].

In this context, AAS is a synthetic derivative of the male hormone testosterone and is commonly abused by athletes and bodybuilders to increase strength and body weight [36]. Strength gains of about five to 20% of the initial strength and increments of two to five kg of body weight, which can be attributed to an increase in body mass [37]. In addition to these positive anabolic effects, AAS has numerous adverse cardiovascular effects when consumed in doses 10 to 40 times the therapeutic doses, such as accelerated atherosclerotic disease that leads to acute myocardial infarction, accidents, dilated cardiomyopathy and sudden death [38].

The exact mechanisms for the adverse cardiovascular effects associated with AAS are still uncertain. Several mechanisms have been proposed and confirmed in animal studies and include increased coagulopathy and platelet hyperactivity [39-41], effects on vasoreactivity, resulting in vasospasm [42, 43], reduced antioxidant activity [44] changes in lipid levels [45, 46]. AAS has been reported to affect hemostasis by both coagulation and the fibrinolytic system. They cause a hypercoagulable state by increasing the production of various clotting factors, such as factors II, V, VIII, and X [42].

At the same time, AAS also increases the plasma concentration of fibrinolytic factors, such as antithrombin III, protein C and S, with reduced levels of plasminogen activator inhibitor, resulting in an increased state of fibrinolysis [41]. Consequently, AAS causes a hypercoagulable state that is counterbalanced by an increase in fibrinolytic activity to maintain hemostasis. This balance between hypercoagulability and increased fibrinolysis caused by AAS is dose-dependent. At therapeutic doses, AAS, such as danazol, has been used in patients with protein S deficiency to reduce the incidence of DVT [47]. However, at high doses, such as those associated with AAS abuse by athletes and weightlifters, the balance can be tilted to a hypercoagulable state, resulting in an increased incidence of thromboembolic events.

The expression of thromboxane A2 (TXA2)/prostaglandin H2 (PGH2) receptors in cultured human erythrocytes (HEL) cells, a megakaryocyte-like cell line, is increased when incubated with testosterone [48]. TXA2/PGH2 receptors are also expressed in platelets, and testosterone has also been shown to regulate the expression of TXA2 platelet receptors in humans [47, 48]. Treatment with 200mg intramuscular testosterone given twice, with an interval of two weeks in human participants, was found to increase platelet TXA2 receptors that peak in four weeks, increasing platelet aggregation response to mimetic 125I-BOP of the TXA2 [48].

Increased platelet sensitivity to collagen has also been found in weightlifters who regularly abuse AAS [40]. Hemoglobin, red blood cell count, hematocrit, and platelet count have been shown to increase significantly during treatment with danazol, an anabolic steroid commonly used in endometriosis [49]. This increase in blood viscosity combined with increased platelet sensitivity and aggregation response in a hypercoagulable environment due to increased clotting factors may explain the thromboembolic side effects seen with AAS abuse in weightlifters and athletes.

Thus, AAS is a synthetic derivative of testosterone and is widely used by the general public to increase lean weight and improve athletic performance. Although there are many related studies, there was no consensus on the use of AAS and cardiovascular risk. In this sense, a study reviewed the effect of AAS on the cardiovascular system and showed that its use and abuse is correlated with higher cardiovascular risks [49].

Finally, another recent study showed that a 34-year-old man was found out of breath and panting at home three hours after a workout at the gym and, minutes later, died. The examination of the heart had left ventricular hypertrophy, while the right coronary artery had only a small vascular lumen (3 mm in diameter). About 1 μg/L clenbuterol, 56 μg/L stanozolol, and 8 μg/L methandienone with trenbolone have been found in the femoral blood. Also, there were positive urine results for boldenone, clomiphene, trenbolone,
methandienone, stanozolol, clenbuterol, and drostanolone. Thus, long-term consumption of AAS caused pathological changes in the heart. Besides, the combination of anatomical risk factors such as small coronary artery and ventricular hypertrophy with the use of AAS can lead to fatal cardiovascular failure [50].

CONCLUSION
According to the literary findings and in resonance as the present case report, the abuse of AAS has a toxic cardiovascular effect, which significantly increases the incidence of cardiovascular diseases such as atherosclerosis, hypertension, myocardial necrosis, heart failure, hypertrophy, thromboembolism, and arrhythmia. Thus, it is necessary to raise awareness about the toxicity of AAS in the general population.

ETHICAL APPROVAL AND CONSENT TO PARTICIPATE
The study was reviewed and approved by the Clinical Institutional Review Board (Approval no. 030438/2020).

HUMAN AND ANIMAL RIGHTS
All the procedures were conducted following the ethical standards laid out in the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

CONSENT FOR PUBLICATION
Informed consent was obtained from the participant included in the study.

STANDARD OF REPORTING
CARE and PRISMA guidelines have been followed.

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AVAILABILITY OF DATA AND MATERIALS
No additional data and materials are available.

CONFLICT OF INTEREST
The authors declare no conflict of interest.

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