

Anabolic steroid induced acute myocardial infarction

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ABSTRACT

Androgenic anabolic steroids are commonly abused by athletes and body-builders to help develop lean body mass and muscular strength to enhance their performance. However, at doses which are much higher than recommended therapeutic dosage, abuse of these drugs is commonly associated with cardiovascular side-effects that can lead to acute myocardial infarction and sudden death. We report here three cases of acute myocardial infarction in local young bodybuilders who were using Stanozolol, an androgenic anabolic steroid, and discuss the pathophysiological mechanisms behind the observed cardiovascular side effects.

Keywords: Anabolic steroids, atherosclerosis, ischaemic heart disease, myocardial infarction, percutaneous coronary intervention, stent, thrombosis

INTRODUCTION

Androgenic-anabolic steroids (AAS) are synthetic derivatives of testosterone and short-term administration by athletes can increase strength and bodyweight.¹ The current regimens of AAS include combinations of injectable and oral preparations taken at doses 10 to 40 times greater than those prescribed therapeutically.² At such high doses, AAS side effects become evident which include vascular complications, coronary atherosclerosis, dilated cardiomyopathy, acute myocardial infarction (AMI) and sudden death.²

Many other adverse effects have been associated with AAS misuse, including disturbance of endocrine and immune function, alterations of the sebaceous system and skin, changes in the haemostatic system and urogenital tract.¹ Three cases of AMI in previously healthy young local bodybuilders in Brunei Darussalam secondary to AAS (Stanozolol) abuse are reported to highlight the dangers associated with these drugs.

CASE REPORT

Case 1: In February 2005, a 30-year-old Malay male bodybuilder was admitted with an inferior AMI. He had no past medical history but during this admission was diagnosed with

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hypertension and hyperlipidemia. He also gave a history of smoking. An urgent coronary angiogram confirmed an acute occlusion of the mid right coronary artery (RCA) by intraluminal clots (Figure 1). As he was stable, he was treated with oral anticoagulation and discharge. Repeat coronary angiogram in May 2005 showed a mid RCA stenosis and a percutaneous coronary intervention (PCI) was performed using a Driver stent, which completely resolved the stenosis. On further enquiry, the patient admitted to using AAS.

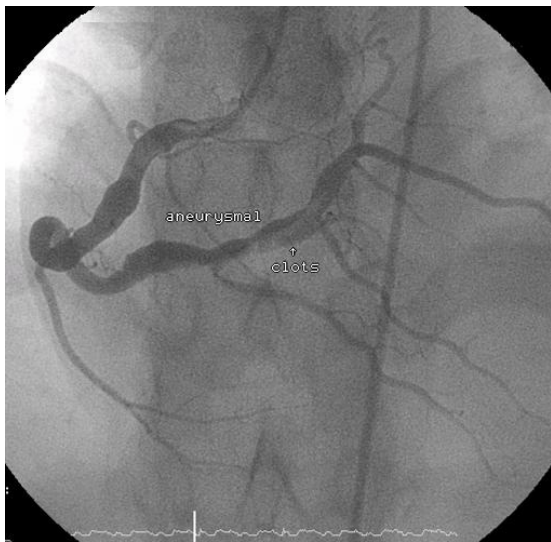


Fig. 1: Large aneurysmal RCA with clots in the distal RCA as indicated by the arrow.

Case 2: In October 2005, another Malay male bodybuilder, aged 46, with a past medical history of hypertension, hyperlipidemia and smoking, was admitted with an antero-inferior AMI. The patient admitted to using AAS. He was treated successfully with thrombolysis and discharged. Subsequently he underwent an elective treadmill test, which was significantly positive and an urgent coronary angiogram confirmed triple vessel coronary artery disease (Figure 2a and 2b). He underwent PCI to all three vessels successfully with three Taxus drug eluting stents

(DES) in November 2005 (Figure 2c and 2d). Follow-up angiogram in January 2006 showed mild stenosis of the left main stem (38%) and restenosis of the mid left anterior descending artery (60%), which was stented with another Taxus DES (Figure 2e and 2f).

Case 3: In December 2005, a 28-year-old policeman who was also a keen bodybuilder was admitted with an anterior AMI. This patient also had used AAS. He underwent immediate thrombolysis but continued to have dynamic ECG changes. Urgent coronary angiogram showed resolution of the occlusion of both LAD and lateral circumflex (LCx) arteries but persistence of luminal RCA clots. All three coronary arteries were pristine in calibre with no luminal disease and hence PCI was not indicated. He was started on warfarin which resolved his symptoms and ECG changes. Blood investigations showed a reduced level of both Protein S and C but absence of anti-cardiolipin antibodies. Subsequent follow-up coronary angiogram confirmed resolution of the RCA clots.

All three patients have been on regular follow up to assess the long-term effects of AAS abuse and to monitor for any signs of dilated cardiomyopathy. They have continued to take part in bodybuilding but have stopped taking AAS.

DISCUSSION

AAS, a synthetic derivative of the male hormone testosterone is commonly abused by athletes and bodybuilders to increase strength and bodyweight. Strengths gain of about five to 20% of the initial strength and increments of two to five kg bodyweight, that may be attributed to an increase of the lean body mass

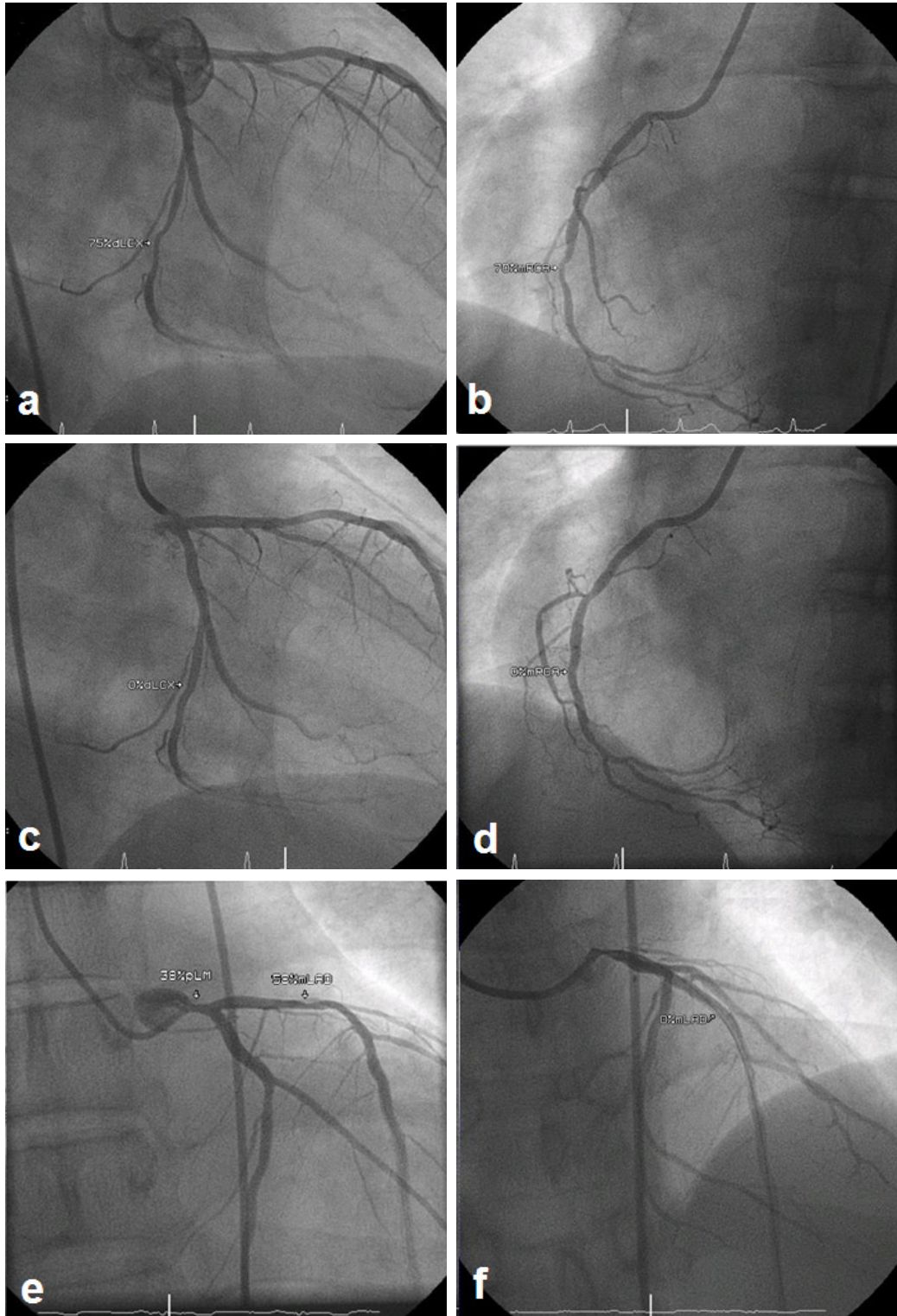


Fig. 2: Angiogram showing significant coronary artery disease in the Cx (a) and RCA (b). PCI with Taxus drug eluting stents were performed successfully (c & d). Recurrence of symptoms and repeat angiogram confirmed mild stenosis at distal LMS (38%) and mid LAD (58%) 2 months after the initial episode (e), the LAD lesion was successfully dilated and stented using another Taxus drug eluting stent (f).

have been observed.¹

Apart from these positive anabolic effects, AAS has numerous adverse cardiovascular effects when consumed in doses 10 to 40 times the therapeutic dose, such as accelerated atherosclerotic disease leading to acute myocardial infarction, cerebrovascular accidents, dilated cardiomyopathy and sudden death.² These three case reports highlight such adverse cardiovascular effects associated with AAS abuse.

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 these include, a) increased coagulopathy and platelet hyperactivity³⁻⁵, b) effects on vasoreactivity resulting in vasospasm^{6,7}, c) reduction in antioxidant activity⁸, and d) changes in lipid levels.^{6,9}

AAS have been reported to affect haemostasis through both the coagulation and the fibrinolytic system. They cause a hypercoagulable state through the increased production of several coagulation factors such as factors II, V, VIII and X.⁵ At the same time, they also increase the plasma concentration of fibrinolytic factors such as anti-thrombin III, Protein C and S with a reduced levels of plasminogen activator inhibitor, hence resulting in a state of increase fibrinolysis.⁴ Consequently, AAS cause a hypercoagulable state which is counterbalanced by an increased fibrinolytic activity to maintain haemostasis. This balance between hypercoagulability and increased fibrinolysis caused by AAS is dose dependent. At therapeutic doses, AAS such as danazol have been used

in patients with Protein S deficiency to reduce the incidence of DVT.¹⁰ However at high doses such as those associated with AAS abuse by athletes and weightlifters, the balance may be tipped towards a hypercoagulable state resulting in an increased incidence of thromboembolic events.

Expression of thromboxane A₂ (TXA₂) /prostaglandin H₂ (PGH₂) receptors in culture human erythroleukemia (HEL) cells, a megakaryocyte-like cell line, is increased when incubated with testosterone.¹¹ TXA₂/PGH₂ receptors are also expressed in platelets and testosterone has also been shown to regulate the expression of platelet TXA₂ receptors in humans.^{11,12} Treatment with intramuscular testosterone 200mg given twice, two weeks apart in human participants has been found to increase platelet TXA₂ receptors which peak at four weeks resulting in an increase platelet aggregation response to TXA₂ mimetic 125I-BOP.¹² Increased platelet sensitivity to collagen has also been found in weightlifters who regularly abuse AAS.³ Haemoglobin, red cell count, haematocrit and platelet count have been shown to increase significantly during treatment with danazol, an anabolic steroid commonly used in endometriosis.¹³ This increase in blood viscosity combined with increased platelet sensitivity and aggregation response in a hypercoagulable environment due to increased coagulation factors may account for the thromboembolic side-effects seen with AAS abuse in weight lifters and athletes.

Another adverse effect of chronic AAS abuse is its effect on vascular reactivity resulting in an increased propensity for vasospasm. This effect on vasoreactivity seen with

AAS has been shown to be due to a potentiation of vasoconstriction responses to epinephrine, serotonin and endothelin-1, combined with an attenuation of vasorelaxant responses to sodium nitroprusside in rabbits.⁶ At a molecular level, testosterone has been shown to increase vascular TXA2 receptor density, resulting in enhanced coronary artery vasoconstriction to TXA2 mimetic in laboratory animals.^{11, 14}

Flow mediated dilatation (FMD) of the brachial artery is commonly measured as a surrogate marker for in-vivo endothelial function. In non-smoking bodybuilders on AAS, FMD was found to be significantly reduced when compared to non-smoking control bodybuilders, indicating impairment of endothelium dependent dilatation.⁷ In this group, endothelium independent vasodilatation using glyceryl trinitrate was also found to be diminished, suggesting that the damage is not just limited to the endothelium but also affects the smooth muscle media.⁷ Endothelial dysfunction is an early indicator of atherosclerosis. The increase in vascular endothelium TXA2 receptors and presence of endothelial dysfunction may account for the finding of systolic hypertension seen in AAS users.

In rats treated with AAS nandrolone decanoate for eight weeks, cardiac tissue levels of antioxidant enzymes superoxide dismutase (SOD), glutathione peroxidase (GPx) and glutathione reductase (GR) activity were found to be significantly lower compared to control rats after a global ischemic event.⁸ Heart infarct size was also significantly larger in AAS treated rats.⁸ This reduction in antioxidant activity may predispose to vascular endothelial damage and accelerated athero-

sclerosis seen with chronic AAS abuse.

The effects of AAS on lipid levels have been well reported both in animal studies and in clinical subjects.^{6, 9} Treatment with testosterone and nandrolone in rabbits is associated with significantly lowering blood HDL levels with a corresponding increase in LDL levels.⁶ AAS cause marked reduction of HDL-C, HDL2-C and HDL3-C levels (weighted average, 52%) and Apo-A1 levels while raising LDL (average of 36%) and Apo-B levels in bodybuilders on AAS, resulting in an increased atherogenic lipid profile.¹⁵

All four pathological mechanisms associated with chronic AAS abuse proposed and proven by animal and clinical studies could result in the development of a prothrombotic and atherogenic state, leading ultimately to early and accelerated atherosclerosis and thromboembolic events such as cerebrovascular accidents or as in our three patients with AMI. Because of the prothrombotic state, myocardial infarction can occur in athletes or body builders with seemingly normal coronary angiograms while in others, in the presence of accelerated coronary atherosclerosis.

In conclusion, it is important for clinicians and general practitioners to be aware of this association and to counsel athletes and recreational bodybuilders carefully regarding this and other side effects that may occur with the abuse of these agents.

ACKNOWLEDGEMENT

I would like to thank Dr Patrick Ang (Gleneagles JPMC) for helping out with the images.

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