

Clenbuterol and Anabolic Steroids: A Previously Unreported Cause of Myocardial Infarction With Normal Coronary Arteriograms

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ABSTRACT: During the last 10 years, several cases of myocardial infarction associated with anabolic steroid use have been reported. Postulated mechanisms to explain this association have included changes in lipid levels, the fibrinolytic system, and platelet aggregation. Clenbuterol is a β_2 -agonist with anabolic properties that has not been seen previously with myocardial infarction. We report a case of myocardial infarction in an otherwise healthy 26-year-old body-builder who recently used clenbuterol and anabolic steroids. In this case, synergistic effects of the two agents seem likely to have played a role in the infarct. The normal coronary arteriograms before any anticoagulant or thrombolytic therapy strongly suggest coronary spasm as the mechanism of the infarct.

SEVERAL REPORTS of myocardial infarction associated with anabolic steroid use have been reported over the last 10 years. The mechanism of infarction remains controversial. Clenbuterol is a β_2 -agonist that has not been previously associated with myocardial infarction. We report the case of a previously healthy 26-year-old man who had an acute myocardial infarction after taking both clenbuterol and anabolic steroids.

CASE REPORT

A previously healthy 26-year-old man with no known risk factors for coronary artery disease came to the internal medicine outpatient clinic with dull, central chest pain of 3 hours' duration. The patient said that he was a competitive body builder who had used anabolic steroids over the previous 3 years. Specifically, he had used intermittent, intramuscular depot injections of testosterone propionate, cypionate, and enanthate, in addition to oral methandrostenolone and stanozolol. He had not used any steroid preparation for 4 weeks before presentation but had since started using oral clenbuterol. The patient was unable to give details of dosing regimes concerning any of the these medications. His only other symptoms were occasional palpitations, tremors, and nervousness over the past 2 weeks.

His medical history was unremarkable, and he denied using tobacco, cocaine, or any other substances of abuse. On examination, the patient was a lean, muscular man in no acute distress, with a blood pressure of 140/90 mm Hg and a pulse rate of 90/min. The remainder of the physical examination was unremarkable. An electrocardiogram

revealed 1-mm ST segment elevation in leads II, III, AVF, and V4 to V6 (Fig 1). Echocardiogram showed dyskinesias of the inferior and posterior wall, normal global ejection fraction, and evidence of left ventricular hypertrophy, with the left ventricular posterior wall measuring 12 mm. After receiving aspirin and nitroglycerin, the patient was sent emergently to the cardiac catheterization laboratory where his coronary angiograms were normal (Figs 2 and 3). The left ventriculogram showed a mildly dilated left ventricle with dyskinesias in the same areas as the echocardiogram.

The patient's cardiac enzymes confirmed a myocardial infarction with a peak creatinine kinase of 1,060 IU/L (normal range, 25 to 190) and MB fraction of 54 ng/mL (normal range, 0.0 to 5.0). His lipid panel was within the normal range. Testing for hypercoagulability with a protein C, S, antithrombin III levels, and factor V Leyden was normal. The remainder of the laboratory data, including a homocysteine level and a urine illicit drug screen, was unrevealing. The patient had an uneventful hospital course. Two weeks after discharge, he was asymptomatic, and an echocardiogram showed resolution of the areas of dyskinesias.

DISCUSSION

It is estimated that in the United States approximately one million people use anabolic steroids each year.¹ Over the past decade, there have been an increasing number of reports of anabolic steroid use associated with cardiovascular entities, including sudden death, ventricular arrhythmia, dilated cardiomyopathy, stroke, arterial thrombosis, and myocardial infarction.²⁻⁴

To our knowledge, since 1988 eight cases have been reported in the English language literature regarding myocardial infarction

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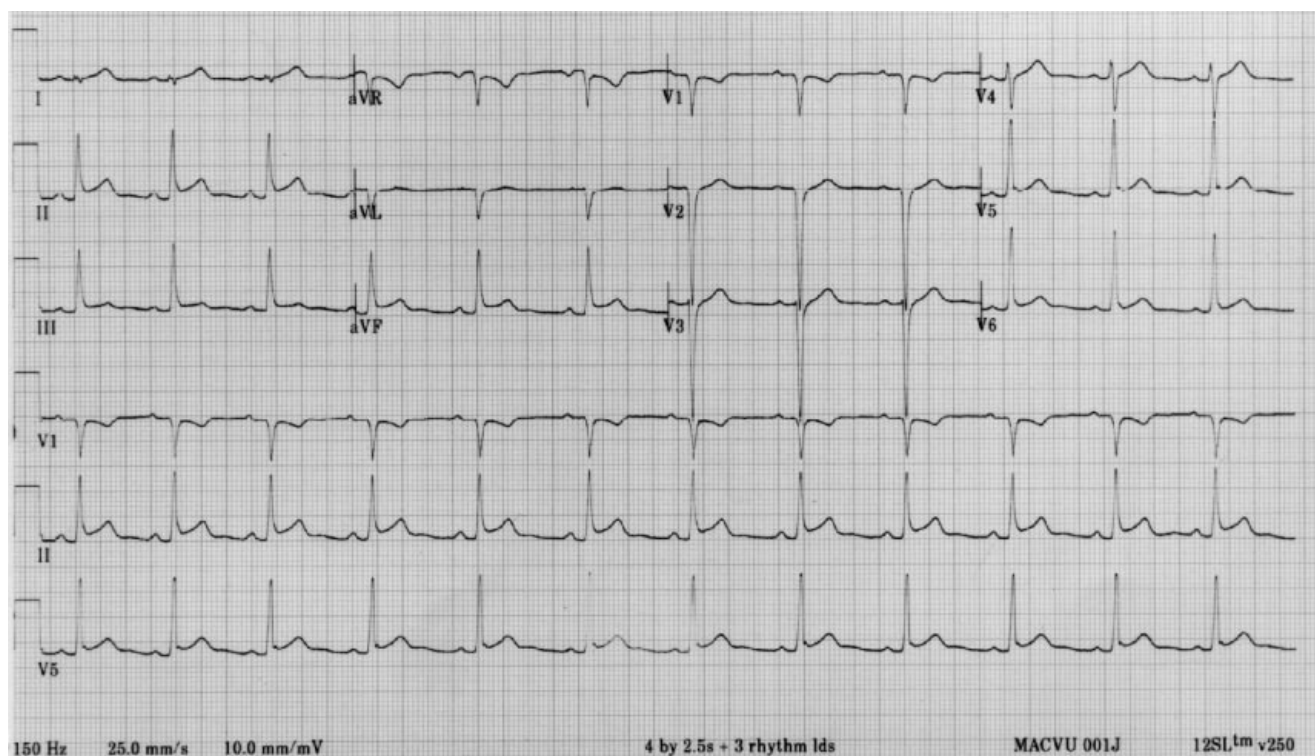


FIGURE 1. Electrocardiogram (12 lead) shows 1 mm ST elevation in leads II, III, aVF, and V4 to V6.

associated with anabolic steroid use.⁵⁻¹¹ The reported patients were young men, generally with a paucity of cardiac risk factors. The timing of steroid use varied from 5 weeks before presentation to use on the day of admission. In one case, high doses of amphetamines were believed to be responsible for the myocardial infarction.⁶ No other substances of abuse were identified in the other cases. Evidence of dyslipidemia was found in three patients who had markedly high low-density lipoprotein (LDL) and low high-density lipoprotein (HDL).^{5,7,9} Thrombolytics were given to four patients.^{7,8,10,11} Six patients had cardiac catheterizations; normal angiograms were noted in two.^{5,8} No patients had primary angioplasty or cardiac catheterization before anticoagulant or thrombolytic therapy. One patient had cardiogenic shock, and another was found to have a dilated cardiomyopathy.^{10,11} Long-term follow-up information is lacking, but there were no deaths during hospitalization.

Various mechanisms have been proposed to account for the association between anabolic steroids and myocardial infarction, though there is no direct evidence. First, there have been several studies that showed anabolic steroids can cause dyslipidemias—notably an increase in LDL and reduction in HDL.¹² Hence, the use of anabolic steroids could be a

risk factor for the development of coronary artery disease. Second, anabolic steroids may cause a hypercoagulable state by altering components of the coagulation and fibrinolytic system. This was suggested by a recent study that showed activation of the hemostatic system in body builders who used anabolic steroids compared with controls who did not use steroids.¹³ Specifically, anabolic steroid users had higher concentrations of thrombin/antithrombin complexes, prothrombin fragments, and d-dimers. Additional evidence has suggested that anabolic steroids can increase platelet aggregation and thereby promote thrombosis.¹⁴ Third, anabolic steroids may cause a reduction in nitric oxide synthesis and may alter vasodilator properties. This disruption in endothelial function may lead theoretically to coronary artery spasm.¹⁵ Finally, there is evidence from case reports and echocardiographic studies that anabolic steroids can cause ventricular hypertrophy.^{2,3,16} Hypertrophy may promote ischemia and infarction in predisposed patients.

Clenbuterol is a potent β_2 -agonist that is used in Europe as an oral bronchodilator. It has improved oral absorption compared with other β_2 -agonists and has a long elimination half-life. This drug has been used in the farming industry for its anabolic and thermogenic



FIGURE 2. Normal coronary angiogram of left coronary artery (right anterior oblique view).

effects, which are mediated via β_2 -receptors. Body builders use the drug illicitly in this country for these effects.

Cases of accidental clenbuterol poisoning after ingestion of bovine liver have been reported from Europe. Manifestations included palpitations, nervousness, tachycardia, and muscle tremors.¹⁷ These effects are thought to be mediated by β_1 -receptors and are propranolol sensitive.¹⁸

There is little data on the cardiac effects of clenbuterol in patients, and there are no reports of myocardial infarction. One study compared the effect of intravenous clenbuterol with salbutamol in nine patients with a history of myocardial infarction. The study found that clenbuterol had a similar, if not better, safety profile than salbutamol.¹⁹ In a recent publication, two body builders were reported to be using the combination of clenbuterol and anabolic steroids.³ One patient was asymptomatic and was shown to have left ventricular hypertrophy by echocardiogram. The other patient, who was reportedly using high doses of clenbuterol, had a monomorphic ventricular tachycardia induced by an exercise test. Subsequently, an echocardiogram

showed a decreased ejection fraction of 30% with left ventricular hypertrophy and dilatation. Myocardial ischemia and infarction were not thought to play a role in either case.

To our knowledge, this case is the first in which myocardial infarction was associated with a combination of anabolic steroids and clenbuterol. We can only speculate regarding the possible mechanisms of our patient's myocardial infarction. The patient had no known traditional cardiac risk factors, though his lipid profile could have been falsely lowered in the presence of a myocardial infarction. Additionally, testing of the patient's coagulation system, as stated previously, was normal. Our patient had a cardiac catheterization within 6 hours of the onset of chest pain, with the intent of primary angioplasty. None of the cases in the literature reported to date have documented such an early cardiac catheterization, and no patient had such a procedure before anticoagulation or thrombolytic therapy. Other than aspirin and nitroglycerin, the patient had no therapeutic manipulations before the coronary angiograms. The fact that the patient had angiographically normal coronary arteries suggests

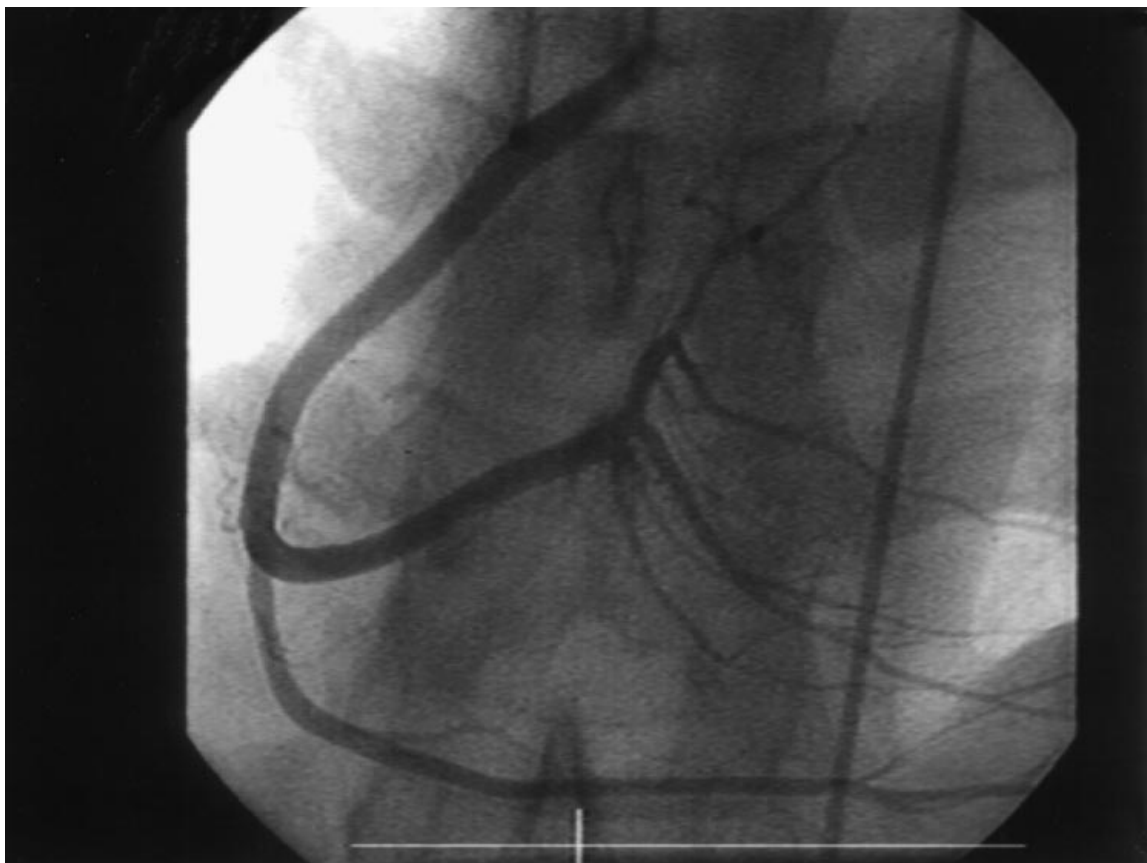


FIGURE 3. Normal coronary angiogram of right coronary artery (left anterior oblique view).

coronary artery spasm as the mechanism of myocardial infarction, though rapidly autolysed coronary thrombus cannot be ruled out. The findings on ventriculography and echocardiography are consistent with transmural ischemia in the distribution of the posterior coronary circulation.

We suspect that there may have been a synergistic role between the anabolic steroid and clenbuterol. Hypothetically, the anabolic steroid may have caused cardiac hypertrophy, coronary artery spasm, or thrombosis. The clenbuterol may have precipitated ischemia by producing intermittent tachycardia. Alternatively, clenbuterol may have contributed primarily to the cardiac hypertrophy by its anabolic effects. Although there is no direct evidence that clenbuterol can cause hypertrophy in humans, recent studies have shown that clenbuterol can cause cardiac hypertrophy in rat models.²⁰ Supranormal doses of either anabolic steroids or clenbuterol could potentially be more pathogenic. Our patient's symptoms for 2 weeks before presentation are suggestive of clenbuterol toxicity. However, it is possible that clenbuterol may have had no pathologic effect.

It is likely that the illicit use of drugs like clenbuterol and anabolic steroids with their health-related consequences will become more prevalent in the future. Young adults appear to be the largest user group, and we are concerned that many users are exposed to other illicit drugs like cocaine, potentially creating an even more hazardous combination.¹ We found it alarming that information about clenbuterol and anabolic steroids could be easily obtained through the world wide web (<http://www.elitefitness.com/steroids/guide.html>).

CONCLUSION

In this case of a myocardial infarction in a healthy 26-year-old body builder who recently used clenbuterol and anabolic steroids, it is difficult to elucidate the contributing roles of each agent, but synergistic effects seem likely to have played a role in the infarct. The normal coronary arteries before any anticoagulant or thrombolytic therapy strongly suggest coronary spasm as the mechanism of the infarct. We urge physicians to ask about these substances when confronted with young patients who have cardiovascular events such

as myocardial infarctions, and we welcome further reports.

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