Myocardial Infarction Associated with the Use of a Dietary Supplement Rich in Ephedrine in a Young Athlete

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Dietary supplements containing ephedrine and other alkaloids related to ephedrine are largely consumed in various countries, with the purpose of energetic stimulation and weight loss. Despite the fact that it is not approved for marketing in Brazil, these products may be freely purchased over the Internet or at gyms/fitness centers. We report the case of a young athlete with no risk factors for cardiovascular disease who experienced a myocardial infarction during the period in which he used an ephedrine-rich supplement.

Ephedrine is a sympathomimetic alkaloid derived from plants of the genus *Ephedra*, with more than 40 species distributed in areas of temperate and subtropical climates. For centuries, its use for therapeutic purposes has been disseminated among the Chinese who used the extract of the dehydrated plant (called *Ma huang*) to treat respiratory ailments[1]. In modern medicine, ephedrine has been used as a nasal decongestant, bronchodilator, and vasopressor[2], but the therapeutic uses of these alkaloids have been restricted because of doubts as to their safety profile.

Currently, dietary supplements that contain ephedrine and other ephedrine-related alkaloids are widely consumed in several countries for the purpose of energy enhancement (to increase athletic performance) and weight loss, in spite of clinical studies that show that this loss is modest and short-lived[3]. Even though its sale is prohibited in Brazil, these products may be bought illegally over the Internet or at gyms/fitness centers. Cardiovascular adverse events such as arterial hypertension, tachyarrhythmias, myocardial infarction, and sudden death with the use of ephedrine are well documented in literature, besides reports of myocarditis associated with the use of ephedrine-containing compounds. It is believed that the vasospasm by α and β-adrenergic stimulation is the mechanism behind both myocarditis[4] and acute myocardial infarction; the adrenergic effects of ephedrine that cause a reduction in the refractory period allow the development of arrhythmias as well. The cardiovascular effect of ephedrine is, at least in part, similar to that of codeine, a drug that also causes α and β-adrenergic stimulation leading to increased blood pressure, increased heart rate, coronary vasospasm, ischemia, infarction, and arrhythmias[5].

We report the case of a young athlete with no risk factors for cardiovascular disease who experienced a myocardial infarction during the period in which he used an ephedrine-rich supplement.

Case report

Our patient is a 28-year-old male, a mixed martial arts fighter, who for some time took Therma-Pro™, a dietary supplement used in order to lose weight before weighing in for the fights. According to the patient, besides the weight loss (up to 12 kg in 20 days, when associated with intense physical training and diet), this product would cause palpitations, tremors, and insomnia. He had used the product before, and always experienced these symptoms. During the period of preparation for a wrestling match, the patient began using four tablets/day of Therma-Pro™, and on the third day developed an intense resting chest pain, described as a tightening sensation, that worsened with effort and improved with rest, with prolonged intermittent duration. He sought medical help, and an analgesic was prescribed to no avail. After six days from the onset of pain, his condition progressed with syncope and hemiparesia on the right, and the patient was seen at other health care centers and referred to our institution merely 30 days after the onset of the clinical picture. On this occasion, that patient had already totally recovered from his motor deficit, but presented with congestive heart failure functional class II (NYHA). He reported no prior history of arterial hypertension, diabetes mellitus, dyslipidemia, or familial history of cardiovascular diseases. He had smoked half a pack of cigarettes a day for five years, but had stopped smoking 3 years prior. He was questioned directly about cocaine use on several occasions during his hospital stay; he denied use of illicit drugs and other stimulants, such as steroids and anabolic products.

On physical examination his Blood pressure was 120/70 mmHg, Heart rate 72 bpm, weight 104 kg, and height, 1.77m. In spite of a body mass index in the obesity range (33.2), he had a large muscle mass and little adiposity.

The test results showed an ECG with an extensive electrically

Key words

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inactive anterior area, normal chest X-ray, total cholesterol 144 mg/dl, HDL 32 mg/dl, LDL 77 mg/dl, triglycerides 176 mg/dl, fasting glucose 78 mg/dL, normal complete blood count, and creatinine 1.5 mg/dl. The echocardiogram revealed a left ventricle (LV) with dimensions at the upper limit of normalcy and a 45% ejection fraction. Segment contraction analysis showed anteroseptal, apical, and anterior akinesia. The presence of a thrombus in the LV was also noted. The patient was submitted to a coronary angiography, that identified an anterior descending artery (DA) occluded at its origin (figure 1A) with mid and distal thirds filling through discreet intracoronary collateral circulation, besides the apical thrombus and a significant increase in LV diastolic pressure. Because of the collateral circulation, angioplasty of the DA with a stent (figure 1B) was chosen. The patient progressed with no complications after the procedure.

Discussion

The incidence of symptomatic coronary disease and acute myocardial infarction (AMI) in young patients under the age of 40 is low - only 3% of cases occur in patients from this age group[6]. Epidemiological studies have shown that the most prevalent risk factors in this population are smoking and a family history of cardiovascular disease. The history taking as to the use of licit or illicit sympathomimetic drugs (cocaine, "crack") should always be very thorough in these cases, especially when no traditional risk factor for atherosclerotic disease is identified. In the case described above, the absence of risk factors and the temporal association between the use of the ephedrine-rich supplement and the occurrence of the acute event suggest a strong causal relationship.

Ephedrine in its pure form and the *Ma huang* extract, rich in ephedrine and other alkaloids similar to ephedrine, such as pseudo-ephedrine, are the usual components of dietary supplements consumed by athletes of different sport modalities who seek a quick weight reduction and an energy boost. They are used indiscriminately, despite warnings from health agencies such as the American Medical Association,[7] and the fact of being considered doping by the majority of sports entities. The use of these products has been associated with several adverse cardiovascular and neurologic events.[8] In April 2004, the United States FDA prohibited the sale of these products and it was the first time the sale of a dietary supplement was banned. In spite of not being a greatly prevalent causal agent, the use of these supplements cannot be excluded in cases of sudden death of young athletes with no structural cardiopathy.[9]

According to data available from the manufacturer, the product used by the described patient, Therma-Pro™ has in its formula 250 mg of *Ma huang* extract, an equivalent to 20 mg of ephedrine. The dose the patient used, four pills a day, is twice that recommended by the manufacturer. Regardless of the dose, ephedrine is a drug that instigates the release of endogenous catecholamines stimulating α-1, β-1, and β-2 adrenergic receptors[10]. The effects of ephedrine are vasoconstriction and cardiac stimulation, leading to an acute rise in arterial blood pressure and heart rate, besides mydriasis, insomnia, vertigo, headaches, and anxiety. Pseudoephedrine causes bronchodilation, because of its primary action of β-2 adrenergic receptor stimulation, while its α-agonist effects are responsible for improving symptoms of nasal congestion.

In the coronary circulation, ephedrine can cause vasospasms[11], especially in individuals with an increased vagal tonus, as was the case of the young man described herein, since he was a physically fit athlete. In many acute coronary syndrome cases associated with the use of ephedrine in patients with normal coronary angiographies, this seems to be the possible physiopathological mechanism[12]. Nevertheless, *in situ* thrombosis may be associated[13] for various reasons: besides slowing the coronary flow, a spasm may cause rupture of the fibrous covering of young atherosclerotic plaques that

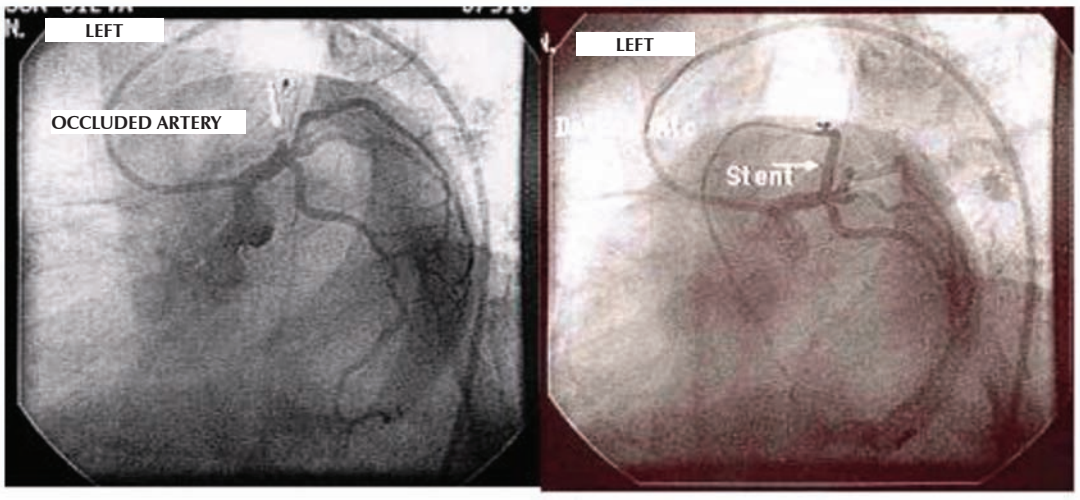

Fig. 1 - *Presence of proximal occlusion in anterior descending artery: before (a) and after (b) angioplasty with stent.*

have an extensive lipid nucleus. In patients who use drugs such as ephedrine, this happens in the presence of significant platelet activation through the sympathomimetic activity of this substance. An association between a spasm and an *in situ* thrombus may have occurred in the case we described, since the coronary angiography showed a complete occlusion of the anterior descending artery, but no evidence that any other vessel had been compromised.

In the absence of prior thrombotic events, whether venous or arterial, and in the presence of a factor that has increasingly been recognized as a cause of acute myocardial infarction (AMI) in young patients, no thrombophilia investigation was made in this patient. Most polymorphisms of the coagulation system proteins involved with venous thrombosis present little or no association with an AMI[14]. In Brazil, Faria-Neto *et al*.[15] demonstrated a low prevalence and no correlation of Factor V Leiden and prothrombin G20210A and methylenetetrahydrofolate redutase C677T (involved in homocysteine metabolism) polymorphisms with the presence of coronary occlusion shown by coronary angiography.

The choice of a late angioplasty of the infarction-related artery in this patient is a controversial treatment option, above all in the absence of a study on the viability of the affected area. Currently, a large study sponsored by the National Heart, Lung, and Blood Institute (NHLBI) is underway to test the hypothesis that the late opening of infarction-related arteries (3 to 28 days after the AMI) with a stent, in high-risk asymptomatic patients (LVEF < 50% and proximal occlusion of a large artery), reduces composite death outcomes, non-fatal recurring infarctions, and functional class IV heart failure (average follow-up of three years)[16].

The description of this case alerts us as to the need to educate the community regarding the risks involved in the use of dietary supplements containing ephedrine that continue to be sold illegally on the premise of a rapid weight loss and enhanced physical performance.

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