Acute myocardial infarction caused by amphetamines: a case report and review of the literature

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Key words:
Acute myocardial infarction; Amphetamine; Calcium channel blockers; Endothelial dysfunction.

Cardiotoxicity manifesting as myocardial ischemia is not generally recognized as a side effect of amphetamine use or abuse. However, at least 9 cases have been reported since 1987. In this report a case of acute myocardial infarction due to oral amphetamine therapy is presented. The patient was treated with thrombolytic therapy but there were no signs of reperfusion. His coronary cine-angiograms were normal.

The literature regarding amphetamine use or abuse is also reviewed, and the possible mechanisms of this pathology are analyzed.

(Ital Heart J 2001; 2 (6): 478-480)

Received December 18, 2000; revision received April 6, 2001; accepted April 19, 2001

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Introduction

Amphetamine use or abuse has been implicated in the pathogenesis of congenital heart diseases and also in the etiology of cardiovascular diseases including cardiomyopathy, cor pulmonale and necrotizing vasculitis[1].

Acute myocardial infarction after amphetamine use has rarely been documented. The present case report involves a patient with myocardial infarction resulting from the administration of oral amphetamines.

Case report

A 34-year-old man, with no history of angina and no familial risk of coronary heart disease, who smoked 20 cigarettes a day, had been undergoing amphetamine therapy without signs and symptoms of amphetamine intoxication (i.e. seizures, hypereflexia) for 1 week in order to lose weight due to a mild form of obesity. No other drugs were used and he had been in good health in the past.

He arrived in our Emergency Department presenting with severe substernal chest pain. An electrocardiogram (ECG) showed ST segment elevation in leads II-III and aVF (Fig. 1). His blood pressure was 130/80 mmHg, and there were no signs of heart failure. He was treated with thrombolytic therapy (tissue plasminogen activator 100 mg front loaded).

A diagnosis of acute myocardial infarction was subsequently confirmed by serial enzyme analysis (peak creatine kinase level 750 U/ml, MB 10%). However, neither serial creatine kinase determination nor ECG revealed reperfusion.

Echocardiography, performed on the day of admission, showed inferior left ventricular hypokinesia; the left ventricular ejection fraction was estimated to be about 50%.

On the fifth day, coronary cine-angiograms were performed revealing normal coronary arteries without any evidence of atherosclerotic plaques, congenital abnormalities or thrombi. However, the inferior left ventricular hypokinesia was confirmed.

Blood and urine toxicological screening was positive for amphetamine metabolites and negative for cocaine metabolites.

An ECG, performed before hospital discharge, showed electrical modifications compatible with a non-Q wave inferior myocardial infarction and, in particular, ST-T segment elevation in leads II-III and aVF persisted (Fig. 2).

During hospitalization, a calcium channel blocker regimen (verapamil 240 mg/day) was begun and subsequently continued at home.

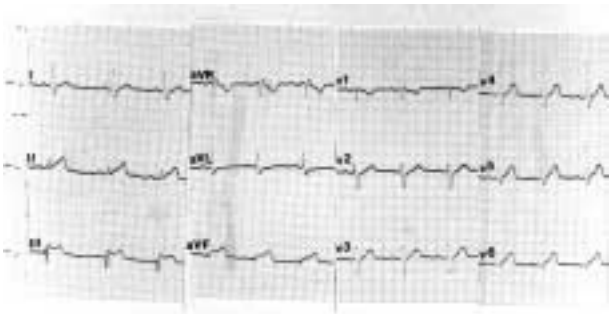

Figure 1. *ECG at admission showed elevation of ST-T segment in leads D_2-D_3-aVF.*

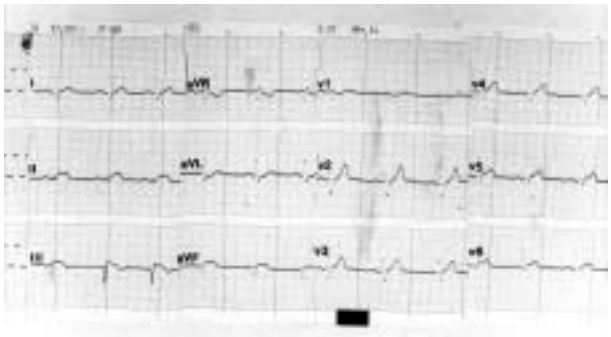

Figure 2. *ECG at discharge showed a pathologic Q wave and persistent ST-T segment elevation in leads D_2-D_3-aVF.*

At follow-up, 3 months after infarction, the patient had stopped smoking, was still taking calcium channel blockers and no longer complained of any chest pain.

Discussion

Our patient sustained an acute myocardial infarction after 1 week of oral amphetamine use. The only cardiovascular risk factor was cigarette smoking, and his coronary arteries appeared normal; the association between amphetamine use and myocardial infarction in our patient is probably not coincidental.

In the literature 9 cases of myocardial infarction associated with amphetamine use have been reported (Table I)[2-9].

Carson et al.[2] described the first case in a 33-year-old patient 1 hour after an intravenous injection of an amphetamine. Rangland et al.[7] described a fatal myocardial infarction after intravenous administration of an amphetamine.

The time interval from the use or abuse of amphetamines to the onset of symptoms varies from a few minutes to years; this variability is probably due to the blood concentration of the drug and to differences in the patients' predisposition to the development of complications.

No specific myocardial site has been localized for the onset of infarction in subjects who take amphetamines; it can be anterior, inferior or lateral.

Of the 9 cases described in the literature, 3 took the drug intravenously, 4 orally and 2 intranasally. The 3 patients who took intravenous amphetamines presented with anterior myocardial infarction.

In all the patients described in the literature, as in our study, there were no other risk factors other than cigarette smoking and only 1 patient was taking other drugs (steroids).

The cause of myocardial ischemia is uncertain even though coronary artery spasm followed by thrombus formation is considered the most likely pathogenetic mechanism. Furst et al.[4] revealed a subtotal occlusion of the right coronary artery in a 41-year-old man who was admitted to the hospital for acute myocardial infarction after intranasal use of amphetamines. Bashour[8] also demonstrated thrombus formation in the proximal left anterior descending coronary artery in a 29-year-old woman who had a history of oral amphetamine abuse.

A thrombus at the level of the coronary artery supplying the infarct area was reported in only 2[4,8] of the cases described in the literature while in the other patients, the coronary cine-angiograms showed coronary arteries devoid of lesions.

Amphetamines stimulate the release of noradrenaline from the sympathetic nerve endings; catecholamines can cause myocardial damage by increasing myocardial oxygen demand and inducing platelet aggregation and coronary arterial vasospasm. The increased cate-

Table I. Characteristics of the patients described in the literature.

Author	Age (years)	Sex	Cardiological risk	Amphetamine administration	Site of infarction	Drugs	Coronary cine-angiogram
Carson et al.[2], 1987	33	M	Tobacco smoking	Intravenous	Anterior-lateral		Normal
Packe et al.[3], 1990	27	M	Tobacco smoking	Intravenous	Anterior	Proclopromazine	Normal
Furst et al.[4], 1990	41	M	Negative	Intranasal	Inferior	Thrombolytic	Thrombosis
Veesntra et al.[5], 1990	25	M		Oral			Normal
Veesntra et al.[5], 1990	40	M		Oral			Normal
Huang et al.[6], 1993	42	M	Tobacco smoking	Intranasal	Anterior	Nitroglycerin	
Ragland et al.[7], 1993	37	F	Tobacco smoking	Intravenous	Anterior	Thrombolytic	Normal
Bashour[8], 1994	29	F	Negative	Oral	Inferior + anterior	Nitroglycerin + heparin	Thrombosis
Appleby et al.[9], 1994	31	M	Tobacco smoking	Oral	Inferior-lateral	Thrombolytic	

cholamine levels could trigger the rupture of an atherosclerotic plaque via their positive chronotropic and inotropic effects. The rupture of an atherosclerotic plaque, coronary arterial vasospasm and platelet aggregation can cause thrombus formation.

The role of amphetamines in inducing vasoconstriction and vasospasm is not completely explained by adrenergic stimulation. Cocaine can play a role by altering the vessel endothelium. Wilbert-Lampen et al.[10] demonstrated in a recent study that cocaine increases the release of endothelium-1 *in vitro* and *in vivo*. It appears to be an exogenous stimulator acting at the level of the endothelial sigma-receptors. The endogenous opioid system plays a role in vasospastic angina, acute myocardial infarction and sudden cardiac death.

Amphetamines exert direct effects on the myocardial cell. These include disorganization of the myofibrillar architecture, edema, vacuolization, mitochondrial swelling and disruption of the intramitochondrial cristae.

The treatment of myocardial infarction arising in the context of amphetamine abuse is not clearly defined at present.

In 3 of the 9 clinical cases reported in the literature[4,7,9], the patients were submitted to systemic thrombolytic therapy. Reperfusion signs appeared in only one of these cases; thrombolytic therapy is a possible strategy but its efficaciousness is still uncertain; as a matter of fact, only 2 patients presented with coronary thrombosis. One of them received thrombolytic therapy and the other was treated with heparin infusion and antiplatelet drugs. It is logical that thrombolytic therapy be performed when a coronary angiogram reveals a pattern suggestive of coronary thrombosis.

Since they may exacerbate vasospasm, beta-adrenergic blocking agents should be avoided until the pathophysiology of amphetamine-related myocardial infarction is established. In fact, Ragland et al.[7] administered an oral propranolol regimen at a dose of 10 mg and, after the second dose, the patient complained of chest pain.

Following intracoronary administration of propranolol to cocaine users, Lange et al.[11] demonstrated a decreased coronary blood flow and an increased coronary resistance.

Calcium channel blockers may play an important role in the treatment of myocardial infarction due to amphetamine use or abuse and, as in our case, may be effective in the treatment of vasospastic angina. In these patients the administration of beta-blockers should be avoided; thrombolytic therapy or intravenous anticoagulants are possible if an arterial coronary thrombus is present and a logical prophylactic regimen consisting of calcium channel blockers and antiplatelet agents is able to prevent the onset of myocardial infarction as a complication of such a clinical situation.

Phentolamine (α_1 and α_2-adrenergic blocking) controls peripheral vasoconstriction but results from sympathetic stimulation due to amphetamines. Refractory cases with significant end-organ toxicity (myocardial ischemia) can be managed with intravenous phentolamine[12].

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