Non–ST-Segment Elevation Myocardial Infarction in the Setting of Sexual Intercourse Following the Use of Cocaine and Sildenafil

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Acute myocardial infarction (MI) in the setting of sexual intercourse following the concomitant use of cocaine, alcohol, and sildenafil has not been previously reported. We present a case of a middle-aged patient with no previous history of angina pectoris or coronary artery disease who presents with severe ischemic chest pain and an MI induced by cocaine, alcohol, sildenafil, and sexual intercourse.
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Key words: Acute coronary care • Aging • Catheterization • Acute coronary syndromes • Myocardial infarction

A 62-year-old African American man presented to the emergency room at 7:00 AM with acute onset of retrosternal, burning, constant, severe, non-radiating chest pain that started 3 hours prior to presentation. The patient had sniffed 1g of cocaine and had several alcoholic drinks 4 hours prior to presentation. He then took a 50-mg tablet of sildenafil and had sexual intercourse 3 hours prior to presentation. During the peak of sexual intercourse,

he developed severe chest pain. He had no previous history of chest pain. Past medical history included diet-controlled type II diabetes mellitus. He also had a history of hypertension but had been noncompliant with medications for 1 month. His hemoglobin A_{1c} level a few months prior to presentation was 6.1%.

On physical examination his blood pressure was 163/103 mm Hg and his heart rate was 88 beats per minute (bpm). He was in acute distress. Cardiac examination revealed normal heart sounds without murmurs, rubs, or gallops. The rest of the physical examination was unremarkable. His presenting electrocardiogram showed normal sinus rhythm at 88 bpm with 1 mm ST-segment depression in the inferior and lateral leads. Echocardiogram revealed concentric left ventricular hypertrophy, normal left ventricular ejection fraction, and no wall motion abnormality.

The patient was suspected of having a non–ST-segment elevation myocardial infarction (NSTEMI). Initial cardiac troponin levels were normal (< 0.1 ng/mL) and creatine phosphokinase (CPK) was 247 units/L (normal < 200 units/L). However, 7 hours after presenting to the hospital, the cardiac biomarkers trended upward to a peak CPK of 5090 units/L, CPK-MB of 414.9 ng/mL (normal $<$ 5 ng/mL), MB% 21.7 (normal $<$ 5), and troponin T of 7.18 ng/mL. Lipid profile revealed a low-density lipoprotein level of 141 mg/dL, high-density lipoprotein level of 52 mg/dL, and triglyceride level of 171 mg/dL.

The patient was given aspirin, 325 mg, atorvastatin, 40 mg, and clopidogrel, 300 mg, and was started on intravenous heparin and eptifibatide drip. A coronary angiogram was performed that revealed a 99% thrombotic occlusion with Thrombolysis In Myocardial Infarction (TIMI) 2 flow in the mid left circumflex artery (Figure 1). The patient also had a 50% and 60% stenosis in the mid and distal left anterior descending coronary artery, respectively. In the right coronary artery, he had a 70% and a 100% stenosis in the proximal and distal portions, respectively, with collaterals from the left coronary artery. A drug-eluting stent was placed in the left circumflex artery (infarct-related artery) after aspiration of the thrombus.

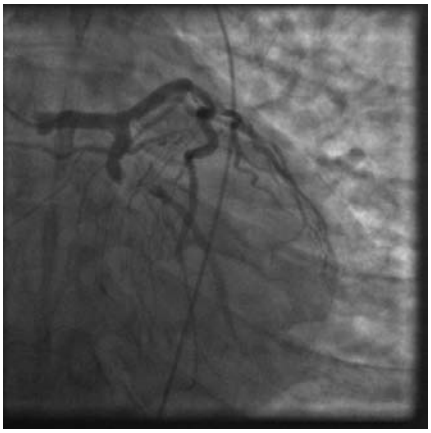

Figure 1. *Coronary angiogram showing thrombotic occlusion of left circumflex lesion.*

Discussion

This was a unique clinical situation in which cocaine, alcohol, sildenafil, and sexual intercourse conjunctively played a role in the development of an NSTEMI.

Erectile dysfunction (ED) is a powerful predictor of cardiovascular morbidity and mortality in diabetic patients with silent coronary artery disease (CAD).[1] ED and CAD share similar pathophysiological mechanisms. The prevalence of ED in the general population varies from 10% to 22%.[1] However, Saha and colleagues[2] have suggested that ED may be present in as many as 50% of men over the age of 40 and that it is primarily due to endothelial dysfunction and the loss of nitric oxide (NO) in the corpus cavernosa.[2] Similarly, endothelial dysfunction has been recognized as an essential component in the development of the atherosclerotic plaque in CAD.[3] Furthermore, ED and CAD are usually coexistent conditions.[3]

Sildenafil is a phosphodiesterase (PDE)-5 inhibitor that is widely used in the treatment of ED. In the normal physiologic state, neurons and endothelial cells of the corpus cavernosa release NO during sexual intercourse. NO activates the enzyme guanylate cyclase within smooth muscle to form cyclic guanosine monophosphate (cGMP). This produces smooth muscle relaxation of the corpus cavernosa and increases penile blood flow. The enzyme PDE-5 degrades cGMP. Sildenafil inhibits PDE-5, and thereby increases levels of cGMP, further enhancing the downstream effects of NO.[4] Sildenafil reaches its maximum plasma concentration within 30 to 120 minutes after ingestion.

Sildenafil can affect the heart in many ways. A report by Saha and colleagues[2] showed that the systolic and diastolic blood pressures decrease by 8.4% and 5.5%, respectively, with the use of sildenafil. Thus, a 40-mg dose of sildenafil in patients with stable ischemic heart disease may decrease cardiac output by 7% and right atrial pressures by as much as 28%.[5] Furthermore, serious cardiovascular events such as MI, sudden cardiac death, ventricular arrhythmia, cerebrovascular hemorrhage, and transient ischemic

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attacks have been reported with the use of sildenafil.[4] This may be related to a drastic lowering of the blood pressure in the setting of other antihypertensive drugs, especially nitrates and α-adrenergic inhibitors.[6] Sildenafil increases circulatory NO concentration, thereby causing vasodilatation and, in the setting of other antihypertensive drugs, may cause a dramatic drop in blood pressure. Sildenafil may also increase coronary vascular shear stress, which may precipitate plaque rupture and induce an MI.[7] Coronary arterial redistribution and hence a steal phenomenon may also develop, in patients with significant coronary disease.[8] There are several reports in the literature (Table 1) showing an association between sildenafil use and MI. In a Phase 1 trial of sildenafil use in England, a cohort of 5000 patients was followed for 5 months; of those, seven had a nonfatal MI and six had a fatal MI.[9] For these reasons, the US Food and Drug Administration has issued a warning regarding the use of sildenafil in patients with preexisting cardiovascular disease. Furthermore, the Princeton Consensus panel has released a consensus statement regarding the use of PDE inhibitors in patients with CAD. For low-risk patients, treatment with these agents is recommended. In patients that are at intermediate risk, exercise stress testing is reasonable prior to initiating these agents. If a patient is classified as high cardiovascular risk, treatment of sexual dysfunction should be deferred until the condition stabilizes. In our patient, his multiple risk factors placed him in the intermediate category and an exercise stress test would have been beneficial.[10]

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Sexual intercourse is a rare trigger of MI (0.5%-1%). During the 2 hours immediately following sexual intercourse the risk of MI increases two- to fourfold.[11] Palmeri and colleagues[12] have shown that sexual intercourse is comparable to stage II of the Bruce Treadmill protocol.[13] As with exercise, sexual intercourse is a stress on the heart; heart rate and blood pressure both rise during sexual intercourse. If significant CAD exists, sexual intercourse may cause ischemia or even an acute MI in the setting of a vulnerable plaque.[3] Sexual intercourse is the precipitating factor in 0.6% of sudden cardiac deaths.[2] Furthermore, cocaine also causes an array of cardiovascular manifestations. Cocaine produces a surge of catecholamines, which increase heart rate, blood pressure, and ventricular contractility, thereby increasing oxygen demand.[14] Cocaine can also promote coronary vasospasm and a prothrombotic effect that may present as an acute thrombus formation or an acute MI.[15] Several case reports in the literature are illustrated in Table 2. There are various case reports of cocaine-induced MI in patients with normal coronary arteries. Weber and associates[16] found that compared with

Table 1
Sildenafil and Acute Myocardial Infarction

Study	Patients (N)	Average Age (Y)	Male (%)	HTN (%)	DM (%)	Smoker (%)	Black Ethnicity (%)	Prior CAD (%)	HL (%)	Culprit Vessel
Mittleman MA et al[13]	69	60	100	37.70	31	NR	8.80	20	22	NR
Hayat S et al[18]	1	50	100	0	0	100	0	0	0	LCX
Arora RR et al[19]	1	70	100	100	0	100	NR	0	100	LAD
McLeod AL et al[11]	1	41	100	0	0	0	NR	0	0	NR
Saha SA et al[2]	1	66	100	100	0	0	100	0	100	LAD
Kekilli M et al[6]	1	45	100	0	0	100	0	0	0	LAD
Muñiz and Holstege[5]	1	44	100	0	0	100	5	0	100	RCA
Feenstra J et al[20]	1	65	100	0	0	0	0	0	0	NR

CAD, coronary artery disease; DM, diabetes mellitus; HL, hyperlipidemia; HTN, hypertension; LAD, left anterior descending; LCX, left circumflex; NR, not reported; RCA, right coronary artery.

Table 2
Cocaine and Acute Myocardial Infarction

Study	Patients (N)	Average Age (Y)	Male (%)	HTN (%)	DM (%)	Smoker (%)	Black Ethnicity (%)	Prior CAD (%)	HL (%)	Culprit Vessel
Weber JE et al[16]	57	43.4	75.40	45.60	8.70	82.40	84.20	0	NR	NR
Mongeon and Rinfret[21]	1	42	100	NR	NR	NR	NR	NR	NR	Left main
Makaryus JN et al[22]	1	46	100	100	100	NR	NR	100	NR	IST
Wilkins CE et al[23]	1	33	100	0	NR	NR	0	0	0	Normal
Inyang VA et al[24]	1	29	100	0	0	100	0	0	0	NR
Villota JN et al[25]	1	26	100	NR	NR	100	NR	NR	NR	LAD
Sachpekidis and Vogiatzis[26]	1	37	100	NR	NR	100	NR	NR	NR	Normal
Coombs M[27]	1	NR	100	NR	NR	NR	NR	NR	NR	Left main
Weiss RJ[28]	1	19	100	NR	NR	NR	NR	NR	NR	60% RCA, 40% LAD
Howard RE et al[29]	1	28	0	NR	NR	NR	NR	NR	NR	Normal
Cregler and Mark[30]	1	38	100	NR	NR	NR	NR	NR	NR	Normal
Pasternack PF et al[31]	1	35	100	NR	NR	NR	NR	NR	NR	LAD, LCX, RCA
Kossowsky and Lyon[32]	6	35.8	100	NR	16.60	50	33	NR	NR	33% LAD, 16% LCX, 16% RCA
Isner and Chokshi[33]	7	28.4	86	0	14	29	0	0	29	14% LAD, 14% RCA, 57% Normal
Majid PA et al[34]	11	27	100	0	0	0	NR	0	0	Normal
Apostolakis E et al[35]	1	28	100	0	0	100	0	0	0	Left main
Montisci M et al[36]	1	31	100	0	0	0	0	0	0	LAD
Singh S et al[37]	4	48	75	25	0	75	100	100	0	IST
Aryana and Mooss[38]	1	49	100	NR	NR	NR	NR	NR	NR	LAD, RCA
Hollander JE et al[39]	49	42.1	84	47	12	96	63	100	29	41% LAD, 59% RCA
Hollander JE et al[39]	21	30.7	76	14	10	95	73	0	14	Normal

CAD, coronary artery disease; DM, diabetes mellitus; HL, hyperlipidemia; HTN, hypertension; IST, in-stent thrombosis; LAD, left anterior descending; LCX, left circumflex; NR, not reported; RCA, right coronary artery.

thrombotic acute MI, cocaine-induced MI patients were less likely to have three-vessel disease, epicardial stenosis was less severe, less thrombus was visualized, and TIMI 3 flow was seen more frequently. Although discrete conclusions cannot be made because of the nature of this study and the lack of a case-controlled prospective study, these findings may support the notion that cocaine-induced MI is its own entity.[16] Furthermore, long-term cocaine use may cause left ventricular hypertrophy and premature coronary atherosclerosis.[14] Cocaine has a half-life of 0.5 to 1.5 hours and its metabolites have half-lives of 3 to 8 hours.[15] Alcohol consumption in conjunction with cocaine use further accentuates deleterious effects of cocaine.[17]

Sexual intercourse and cocaine are known triggers of acute MI and with the concomitant use of sildenafil, the effects on the heart are accentuated.

In this case it could be postulated that the norepinephrine-mediated vasoconstriction and prothrombotic effect caused by cocaine use was accentuated by alcohol consumption and in the setting of sexual intercourse, as a catecholaminergic state, was superimposed by sildenafil's ability to cause coronary steal and increase arterial shear stress, thus causing an acute MI. Sexual intercourse and cocaine are known triggers of acute MI and with the concomitant use of sildenafil, the effects on the

heart are accentuated. Patients should be warned regarding the use of cocaine and sildenafil together in the setting of sexual intercourse. ■

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Main Points

- This is the first reported case of acute myocardial infarction in a patient with concomitant use of sildenafil, cocaine, and alcohol in the setting of sexual intercourse.
- Sildenafil and cocaine use prior to sexual intercourse may accentuate already known triggers for myocardial infarction.
- Patients should be warned regarding using sildenafil and cocaine in conjunction with sexual intercourse.