Phentolamine Therapy for Cocaine-Associated Acute Coronary Syndrome (CAACS)

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ABSTRACT

Introduction: The emergency department (ED) evaluation of cocaine-associated acute coronary syndrome (CAACS) is often a diagnostic and therapeutic challenge.

Case report: We are reporting on the treatment of a patient with cocaine-associated acute coronary syndrome (CAACS) who did not benefit from standard therapy, but who eventually responded positively to phentolamine, an alpha-adrenergic receptor antagonist.

Discussion: This report should encourage physicians to add phentolamine to their pharmacotherapeutic armamentarium in the treatment of CAACS.

INTRODUCTION

Cocaine abuse accounts for over 64,000 ED visits annually, of which more than 50% are chest pain related [1,2]. The differential diagnosis of cocaine-related chest pain is broad and includes acute coronary syndrome (ACS), aortic dissection, pneumothorax, pneumomediastinum, pneumopericardium, and pulmonary infarction [3–8]. Diagnostic and treatment strategies are similar to that of other ED patients with chest pain. However, when considering the therapy of CAACS, strategies differ. For cocaine exposure, coronary artery vasoconstriction is mediated by alpha-adrenergic stimulation [5]. We are presenting the second published case of CAACS with electrocardiogram (ECG) abnormalities that resolved when the use of an alpha-adrenergic receptor antagonist, phentolamine, was implemented.

CASE REPORT

A 43-year-old man with a history of depression presented to the emergency department (ED) with a chief complaint of left sided chest pain that began 1 hour after insufflating cocaine. The pain was described as an intense ache that was a "10 out of 10" in terms of its intensity, and it radiated to his left shoulder. He attempted to alleviate his symptoms by drinking ethanol to "bring him down" but this was unsuccessful at relieving the pain. A similar event happened two weeks prior, also during cocaine use, and the patient was admitted to a hospital and diagnosed with CAACS. His evaluation (including serum troponin levels over a 24-hour period, echocardiogram, and exercise stress test) was normal. He was discharged on aspirin, diltiazem, nitroglycerin, and referred to a

Keywords: cocaine, acute coronary syndrome, phentolamine, toxicity

Notes: Presented at European Association of Poison Centers and Clinical Toxicologists (EAPCCT) XXIV International Congress. Strasbourg, France. June 2004. There was no outside funding of any kind used for this study.

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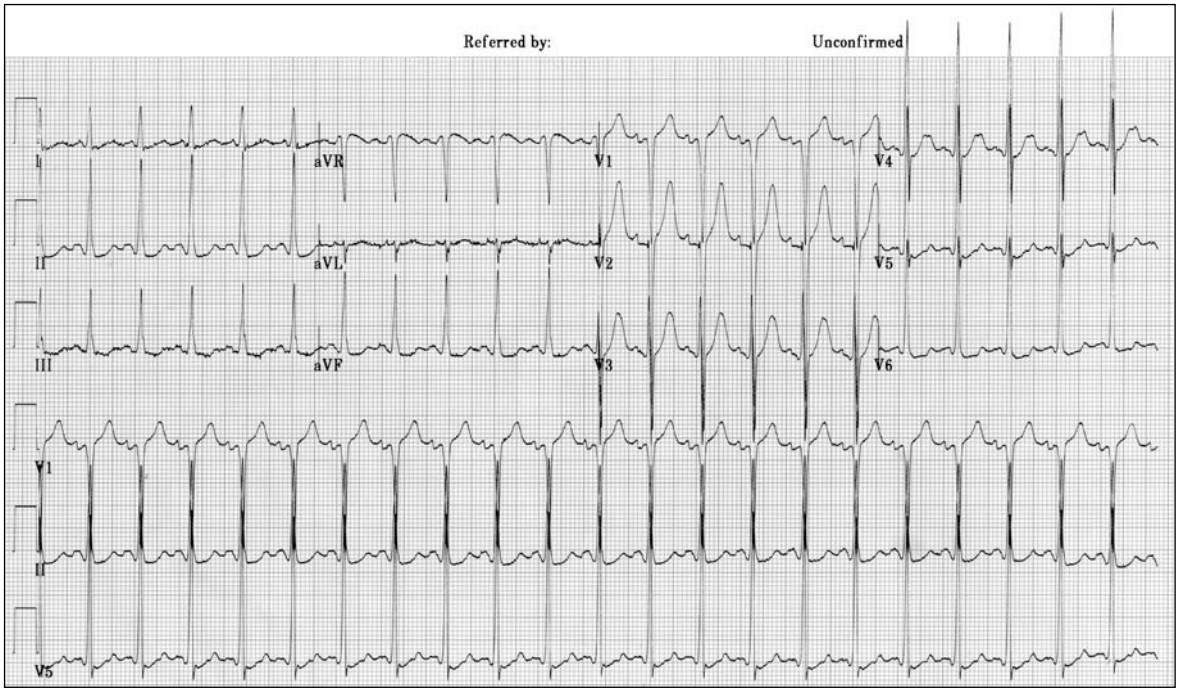

Figure 1. Electrocardiogram on presentation.

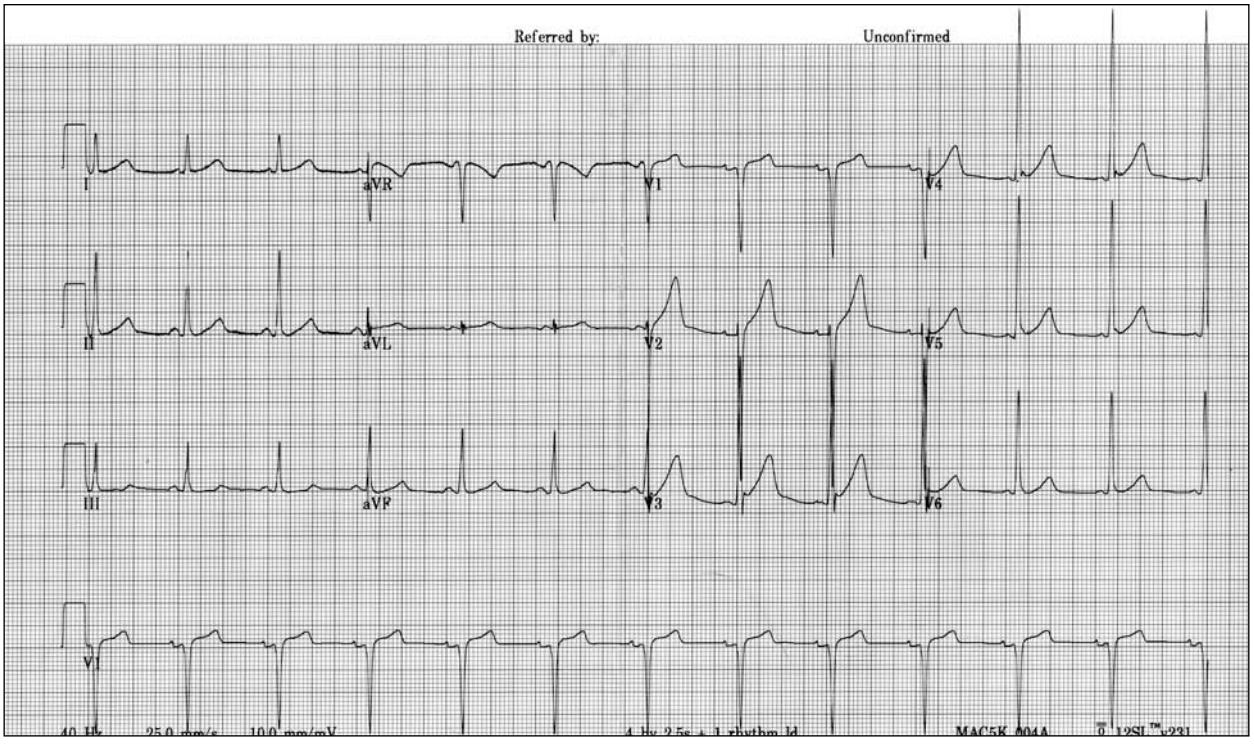

Figure 2. Electrocardiogram after phentolamine administration.

cardiologist for follow-up and a cocaine abstinence assistance program.

The patient took 50 mg of sertraline daily for depression. He used ethanol and cigarettes on a daily basis, occasionally used cocaine, and denied any history of surgery or family medical problems.

On presentation, the patient had the following vital signs: BP, 160/92 mmHg; HR, 130/min; RR, 22/min; Temp, 98.9°F; O_2Sat: 98% on room air and supplemental oxygen was administered per standard protocol via nasal cannula. He appeared anxious and hypervigilant. Head and neck examination revealed dilated pupils (5–6 mm) and moist mucous membranes. His heart was tachycardic with a regular rhythm and lacked any murmur or gallop. His chest was clear, and his abdomen was normal. Extremity examination revealed flushed diaphoretic skin and strong equal pulses. A neurological examination was normal.

A 12-lead ECG showed sinus tachycardia, peaked T-waves in the precordial leads, and ST-segment depression in leads V5 and V6 (*Figure 1*). A portable chest radiograph was interpreted as normal. The ED physician assessed that this patient was sympathomimetic as a result of cocaine use and was experiencing CAACS. The patient orally received 325 mg of aspirin, sublingually received 400 mcg of nitroglycerin, and intravenously received 10 mg of diazepam. After a total of 1.2 mg of sublingual nitroglycerin, the initiation of a nitroglycerin infusion, 40 mg of intravenous diazepam, and 10 mg of intravenous morphine, the patient remained symptomatic with persistent ECG abnormalities. The patient received 1 mg of phentolamine by intravenous bolus at 5-minute intervals for a total dose of 3 mg. Within five minutes of the administration of the last dose of phentolamine, the patient's symptoms and ECG abnormalities resolved (*Figure 2*). The sequence of events is summarized in *Table 1*.

The patient was admitted to a telemetry unit. His serial serum troponin levels (3 tests) were normal over the next 24 hours. An echocardiogram and a dobutamine stress test were also normal. Upon discharge he was offered rehabilitation for his cocaine addiction and was given the discharge diagnosis of CAACS. He has failed to keep any of his outpatient follow-up appointments.

DISCUSSION

Cocaine exposure results in enhanced platelet aggregation and increased circulating catecholamines, each of which increases the likelihood of developing CAACS. Catecholamine excess is a result of reuptake inhibition of biogenic amines such as norepinephrine, epinephrine, dopamine and serotonin [9,5,5]. These neurotransmitters result in beta adrenergic receptor stimulation (which increases myocardial oxygen demand) and in alpha adrenergic receptor stimulation (which results in coronary vasoconstriction) [5]. Diseased coronary segments may be more sensitive to cocaine and experience a greater degree of vasoconstriction [10]. Decreased coronary artery diameter can occur as an effect of the parent compound, cocaine, and some of its metabolites [11].

CAACS requires rapid evaluation and treatment. Its therapy differs from ACS in a few respects. The use of benzodiazepines is recommended in addition to standard ACS therapy because of its ability to suppress catecholamine release via the sympathetic nervous system, which reduces mortality [12,12,13,12,10]. Another notable difference is the absolute contraindication of beta-adrenergic receptor and combined alpha-beta adrenergic receptor antagonists, such as labetolol. This stems from the potential for unopposed alpha-adrenergic agonism that may result in both hypertension and coronary artery vasoconstriction [12,15]. Despite using standard therapies, coronary vasoconstriction and myocardial ischemia may persist.

TABLE 1. Sequence of events

Time From Admission	Therapy	Result
0:00	Oxygen 4L via nasal cannula Aspirin 325 mg orally Nitroglycerin 400 mcg sublingually Diazepam 10 mg intravenously	160/92 mmHg and 130/min; no change in symptoms or ECG
0:05	Nitroglycerin 400 mcg sublingually Morphine 5 mg intravenously	No change in signs, symptoms or ECG
0:10	Nitroglycerin 400 mcg sublingually Diazepam 10 mg intravenously Morphine 5 mg intravenously	No change in signs or ECG, patient experienced mild sedation
0:15	Diazepam 20 mg intravenously Nitroglycerin infusion initiated	No change in signs or ECG, the patient became more sedated
0:20	Phentolamine 1 mg intravenously	152/88 mmHg and 120/min; his pain improved but was still present
0:25	Phentolamine 1 mg intravenously	146/92 and 112/min; pain persisted
0:30	Phentolamine 1 mg intravenously	132/80 mmHg and 72/min; complete resolution of pain ECG resolution (See Figure 2.)

Other agents, in particular, labetolol, have displaced phentolamine—once a readily used pharmacotherapy for hypertensive crisis and pheochromocytoma. Other indications for phentolamine include the prevention of dermal necrosis from extravasation of norepinephrine infusions or following unintended epinephrine autoinjector discharge. Phentolamine is available for intravenous and intramuscular use and has a half-life of approximately 18 minutes. Its potential adverse effects are primarily related to arterial vasorelaxation and include hypotension with resultant tachycardia and potential dysrhythmias. However, when titrated in small increments, this drug can be safely utilized.

When standard therapy for CAACS fails, phentolamine, an alpha-adrenergic receptor antagonist, can be intravenously administered in 1 mg aliquots at 5-minute intervals. Phentolamine administration should stop when either hypotension or relief of symptoms occur. This agent successfully reversed coronary vasoconstriction in cocaine-exposed human volunteers [16]. The effective use of phentolamine in CAACS is previously demonstrated in a single human case report [17].

Even with aggressive ED management, cocaine-induced myocardial ischemia may progress to myocardial infarction. This may perhaps be a result of limited pharmacologic interventions or delayed clinical presentations. This report should encourage ED physicians and cardiologists to add phentolamine in cases of CAACS because it may reverse coronary artery vasoconstriction and alleviate myocardial ischemia.

The author has no potential financial conflicts of interest to report.

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