CASE REPORT

Prolonged cardiac arrest complicating a massive ST-segment elevation myocardial infarction associated with marijuana consumption

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Recreational substance use and misuse constitute a major public health issue. The annual rate of recreational drug overdose-related deaths is increasing exponentially, making unintentional overdose as the leading cause of injury-related deaths in the United States. Marijuana is the most widely used recreational illicit drug, with approximately 200 million users worldwide. Although it is generally regarded as having low acute toxicity, heavy marijuana usage has been associated with life-threatening consequences. Marijuana is increasingly becoming legal in the United States for both medical and recreational use. Although the most commonly seen adverse effects resulting from its consumption are typically associated with neurobehavioral and gastrointestinal symptoms, cases of severe toxicity involving the cardiovascular system have been reported. In this report, the authors describe a case of cannabis-associated ST-segment elevation myocardial infarction leading to a prolonged cardiac arrest.

Keywords: marijuana; myocardial infarction; cardiac arrest; ventricular fibrillation

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intoxication events involving marijuana, alcohol is also detected in the toxicology screen of these patients (2, 3, 20). In a large study, Elmer et al. reported that 14% of out-of-hospital cardiac arrests were deemed to be recreational drugs overdose-related with opiates and benzodiazepines followed by cocaine, methadone, and marijuana being the most common drugs isolated from these patients’ toxicology screens (21). This report describes a patient who developed a prolonged cardiac arrest as a consequence of an ST-segment elevation MI associated with marijuana consumption, ultimately leading to brain death.

Case presentation

A notification was given by the Emergency Medical Service (EMS) to the ED in our hospital regarding a 40-year-old male who developed tonic–clonic seizures followed by cardiac arrest while at a party. When EMS arrived at the scene, a ventricular fibrillation rhythm was recorded and electrical cardioversion was delivered seven times followed by the administration of intravenous amiodarone. Advanced Cardiac Life Support (ACLS) was initiated, which lasted about 40 min. His past medical history was unremarkable, except for recreational drugs use. There was no documented family history of premature ischemic heart disease. On arrival to ED, blood pressure was not able to be registered, but his heart rate was 104 beats/min with regular rhythm. His oxygen saturation by pulse oximetry was 87% despite receiving a fraction of inspired oxygen (FiO2) of 100%. Aggressive resuscitation with vasoactive drugs including norepinephrine, epinephrine, and dobutamine was initiated. Remarkable laboratory findings included a white blood cell count of 18,800/mm3 (4.8–10.8), a lactic acid level of 15.3 mmol/L (0.5–2.2), a blood glucose level of 433 mg/dl (65–115), and a bicarbonate level of 14 mmol/L (24–31). Arterial blood gas (ABG), while on mechanical ventilation and receiving an FiO2 of 100%, showed a pH of 7.02 (7.35–7.45), a pCO2 level of 66 mmHg (35–45), and a paO2 level of 100 (80–100). Troponin I and creatine kinase levels were elevated at 8.32 ng/ml (<0.1) and 2,799 U/L (25–215), respectively. Urine toxicology screen was positive for THC but negative for cocaine, amphetamines, barbiturates, benzodiazepines, methadone, or opioids. A qualitative urine mass spectrometry (Quest Diagnostics Nichols Institute) was negative for synthetic cannabinoids. Serum ethyl alcohol level was 119 mg/dl (<10). Liver function, creatinine, lipid panel, and coagulation profiles were within normal limits. Initial chest radiography showed bilateral infiltrates consistent with pulmonary edema (Fig. 1). A 12-lead electrocardiogram (ECG) demonstrated sinus tachycardia, with ST-segment elevation in leads II–III and aVF as well as V1–V5 (Fig. 2). Transthoracic echocardiogram displayed severely depressed left ventricular ejection fraction of 20% (55–65), global hypokinesis with apical septal akinesia, and a 3.14 cm2 non-mobile, calcified apical thrombus (Fig. 3). Therapy with aspirin, clopidogrel, and intravenous heparin was initiated. Thrombolytic therapy was not considered because of the prolonged cardiopulmonary resuscitation (CPR) time. He was admitted to the intensive care unit (ICU) with the presumptive diagnosis of cardiogenic shock secondary to ST-segment elevation MI. According to the hospital policy, the presence of severe persistent hypoxemia and refractory hypotension despite the use of two vasopressors was considered as the exclusion criterion to initiate therapeutic hypothermia protocol. Within 48 h, hospital course was complicated by worsening kidney function, and severely depressed Glasgow Coma Scale despite being off sedation. Neurological examination disclosed findings compatible with possible diagnosis of brain death: dilated and fixed pupils, absence of corneal and gag reflexes, negative response to deep painful stimuli, no spontaneous breathing, and negative eye-caloric test. Head computed tomography showed diffuse loss of gray-white matter differentiation and ventricular effacement, compatible with global anoxic encephalopathy. No ischemic infarcts or hemorrhage was identified. Given the possibility that the initial neurological examination may had been confounded by the presence of central nervous system depressant drugs, a second neurological assessment was performed in the setting of a negative urine toxicology screen. The results were unchanged. On day 3 of ICU admission, a positive apnea test confirmed the diagnosis of brain death. Autopsy report revealed an acute anterior–lateral, septal, and posterior wall MI with a mural thrombus in the left ventricle as well as hypertensive and atherosclerotic heart disease as the main causes of death.
Discussion
It is difficult to establish the cause-effect relationship between marijuana use and cardiovascular disease. A review of the literature was undertaken to compare our case with other reported occurrences of cannabis-related MI. A MEDLINE search using the words “marijuana” AND “myocardial infarction” yielded 36 cases of acute coronary events likely triggered by the consumption of marijuana. The majority of these patients were male (33, 92%) with a mean age of 30.9 years (median 30, range 17–51), and eight patients (22%) died. A similar search using the words “cardiac arrest” AND “sudden cardiac death” AND “marijuana” resulted in 30 reported episodes. Similarly, most of these patients were male (28, 93%) with a mean age of 34.6 years (median 31, range 15–61). In eight patients (27%), other recreational drugs were also found in toxicology screen (in five of these patients (63%), serum alcohol levels were positive). Twenty-five patients (83%) died. An acute cardiovascular event was the probable cause of death in all these subjects. Summary of cases of cardiac arrest and sudden cardiac death related to marijuana consumption is shown in Table 1. The patient described in this report paired the characteristics of those previously reported events: male gender, young adult, positive serum alcohol levels, and had an unfavorable outcome. Unfortunately, our patient was not able to be transferred to another institution for coronary angiography and possible percutaneous angioplasty because of his hemodynamic instability and elevated FiO2 requirements. As previously outlined by Elmer et al., patients with recreational drug-related out-of-hospital cardiac arrests are less likely to undergo cardiac catheterization (21). It is possible that our patient might have had a non-diagnosed underlying coronary artery disease that may have been aggravated by the consumption of marijuana. This may be supported by the presence of a calcified apical thrombus, which suggests chronicity. It has been suggested that consumption of THC may worsen coronary ischemia in patients with baseline coronary artery disease, potentially triggering an MI (8).

The pathophysiological effects of marijuana in the cardiovascular system are well described, and they seem to be mediated by stimulation of the sympathetic nervous system through release of norepinephrine as well as by parasympathetic nervous system blockade (26). However, the mechanism underlying the association between marijuana use and MI has not been well established. It has been demonstrated that consumption of marijuana increases oxygen demands on the myocardium, leading to an increase in carboxyhemoglobin levels resulting in decreased oxygen-carrying capacity (27, 28). The rise in norepinephrine levels resulting from sympathetic stimulation reduces the left ventricular ejection time, thereby
lowering the threshold for angina. Interference with the integrity of peripheral vascular reflex responses and vascular inflammation with the subsequent increase in platelet activation have been also proposed as mechanisms responsible for cardiac events among cannabis users (29, 30). Reversible vasospasm seems to be the most commonly suggested etiology for cannabis-associated acute coronary syndromes. One study showed that cardiovascular complications resulting from the consumption of marijuana have a mortality rate of about 25% (31). In a large epidemiological study, THC and its derivatives were reported to increase the risk of MI by 4.8 times in the first hour after use (32). Another cohort showed that in marijuana consumers, the population attributable fraction for MI after use (32). Another cohort showed that in marijuana consumers, the population attributable fraction for MI after use (32). Another cohort showed that in marijuana consumers, the population attributable fraction for MI after use (32). Another cohort showed that in marijuana consumers, the population attributable fraction for MI after use (32).

It is unclear why our patient developed seizures before going into cardiac arrest. The relation between marijuana use and epileptic seizures is still controversial. Although cannabis is not commonly associated with seizures and may actually have medical use benefits for the treatment of epilepsy (34), there have been reports of seizures resulting from acute THC intoxication (2, 3). Even though prolonged cardiac arrest leads to hypoxia, which may result in seizures, we do not consider hypoxemia to be the leading cause of seizures in this case given the initial cascade of events, since our patient was initially presented with tonic-clonic seizures that were followed by a cardiac arrest. It is possible that our subject developed seizures because of the synergistic effect of marijuana and alcohol consumption (35). It is also feasible that the patient described in this report might have been under the effects of other recreational drugs unable to be identified by using conventional toxicology screens. Seizures have been reported to be a frequent feature of synthetic cannabinoids intoxication (36, 37). Unfortunately, we were not able to collect any analytical data on synthetic cannabinoids from our patients’ serum except from a negative urine toxicology assay. Our subject’s urine toxicology screen failed to detect the presence of synthetic cannabinoids, making the role of these substances unlikely in our patient’s clinical presentation. We hypothesized that the development of cardiac arrest in our patient was the result of an extensive ST-segment elevation MI, in conjunction with the ventricular fibrillation likely triggered by myocardial ischemia. It is possible that the onset of ventricular fibrillation may have been provoked by tonic-clonic seizures, as previously reported in few other cases (38, 39). As a consequence of the prolonged CPR time and hypoxemia, severe global anoxic brain injury was developed that led to brain death.

There have been previous similar reports of sudden cardiac deaths related to marijuana consumption. Dines et al. reported an 18-year-old male who succumbed to an asystole cardiac arrest while smoking marijuana and suffered hypoxic brain injury related to prolonged cardiac arrest (2). Similarly, Hartung et al. described a 23-year-old male who collapsed with ventricular fibrillation and died after 40 min of unsuccessful CPR (17). In a large cohort of patients with recreational drug overdose-related out-of-hospital cardiac arrests, brain death accounted for more than 30% of fatalities (21). Ventricular fibrillation has been sporadically reported as a result of marijuana consumption (2, 16). A possible explanation for the onset of ventricular dysrhythmias is that cannabis may increase the activity of the Purkinje fibers system (6, 40). The combination of alcohol with marijuana could potentially increase the cardiac toxicity and arrhythmogenic effects of THC by alteration of atrial refractoriness and conduction velocity.

Our report has two potential limitations: first, the initial ECG strip recorded by EMS showing ventricular fibrillation was not able to be recovered, so it is difficult to comment on the rhythm obtained after electrical cardioversion was delivered; second, no blood levels of

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**Table 1.** Summary of cases of cardiac arrest and sudden cardiac death associated with consumption of marijuana

| Reference         | Age, gender | Outcome |
|-------------------|-------------|---------|
| Lindsay et al. (8)| 48, M       | Survived|
| Casier et al. (16)| 52, M       | Dead    |
| Montisci et al. (24)| 31, M   | Dead    |
| Diffley et al. (22)| 15, M   | Survived|
| Menahem (18)     | 21, M       | Survived|
| Bachs et al. (19)| 39, M       | Dead    |
| Hartung et al. (17)| 23, M   | Dead    |
| Tormey (20)*     | 17, F       | Dead    |
| Daisley et al. (23)| 18, M   | Dead    |
| Montisci et al. (24)| 31, M   | Dead    |
| Sattout et al. (25)| 15, M   | Survived|

*F, Female; M, male.

*Autopsy cases.
THC were obtained on admission and, therefore, it may be difficult to attribute the etiology of this acute coronary event directly to the consumption of marijuana. Postmortem toxicological tests were not performed. A positive urine toxicology screen for THC may be insufficient evidence in the linkage of cardiac arrest and marijuana. THC analysis in blood samples must be considered an essential requirement to estimate and correlate the time of last intake with the occurrence of acute cardiovascular events. Unfortunately, the association of marijuana consumption and the occurrence of cardiovascular events is rarely supported by an exhaustive toxicological examination and, when such investigation is performed, it is usually limited to a positive urine toxicological examination that is not reliable for the estimation of the time of last marijuana intake. In this case, as in majority of the previously reported events, the cannabis causality was assumed based on the result of a positive urine toxicology screen for THC and the absence of other substances known to be linked to acute coronary syndrome.

Conclusion
Despite the widespread use of marijuana, public awareness of the risk for potential cardiovascular complications remains low. Although uncommon, severe cardiovascular toxicity and death may develop from its consumption. Further investigations of clinical, toxicological, and epidemiological aspects are needed to enlighten causality between consumption of THC and acute cardiovascular events. Clinicians should be aware of these potential life-threatening complications resulting from the consumption of cannabis.

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