

Marijuana Induced Coronary Vasospasm

Syed Iftikhar, Asma Jamil, Javad Savoj, Rajesh Gulati*

Department of Internal Medicine, Riverside Community Hospital/UCR School of Medicine, USA

***Corresponding author:** Rajesh Gulati, Department of Internal Medicine, Riverside Community Hospital/UCR School of Medicine, USA. Tel: +19517883252; Fax: +18558723252; Email: rgulati@medsch.ucr.edu

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Abstract

Marijuana has become one of the most commonly used recreational drug. Much of its use, is based upon its belief that it is relatively “safe” especially when compared to other drugs. This case, among others, highlights the fact that although marijuana has been utilized for many years in many cultures for many medical reasons, it does not come without risk. Specifically, we like to focus on cardiovascular risk associated with marijuana use. Relatively speaking, extensive research has not been done to localize marijuana and the specific mechanisms by which it can cause cardiovascular morbidity and mortality. However, it is also not an undocumented phenomenon. There have been varieties of case reports as well as studies, which have studied the cardiovascular toxicity, which are associated with marijuana use. Such toxicities include that of Acute Myocardial Infarction (AMI), vasospasm, LV thrombus among others. Here we present one such presentation of a patient with coronary vasospasm presenting as NSTEMI soon after heavy marijuana use.

Introduction

Of all the known “recreational drugs” which are commonly used by the public, marijuana has the highest rate of use, with approximately 4.0 million individuals in the US being considered for marijuana use disorder. This phenomenon is partially derived from the belief that marijuana is generally a benign drug, which does not present physiological effects beyond its well-known psychotropic effects

This belief, however, is unfounded. Marijuana has been documented to have many documented deleterious effects in a variety of organ systems, including the cerebrovascular and cardiovascular systems. There are many hypotheses as to why such effects are visualized in these individuals, ranging from cellular mechanisms involved with Cannabinoid receptors to physiologic sympathetic and parasympathetic responses [1]. One such deleterious phenomenon, which has recently been noticed, is that of cannabis induced coronary vasospasm. Such a phenomenon has been identified and recently documented in a handful of case reports and has generally been noted in young, otherwise healthy individuals without other cause for vasospastic events [2,3].

Here we present a case of a young male with no other risk factors for coronary artery disease, who presented with symptoms of Acute coronary event within 1 hour of heavy marijuana use.

Case Presentation

A 32 y/o M with no known past medical history presented with acute, sudden onset crushing substernal chest pain, which radiated to his left shoulder. This was associated with nausea and diaphoresis. He stated that he had never experienced any similar episodes in the past, and that he was unaware of any premature heart disease. of note, however, was that he stated that less than 30 minutes prior to this current episode, he had heavily smoked marijuana. He stated that he was a regular smoker, however he smoked a much larger amount than was usual for him. He denied using any other recreational drugs such as cocaine or methamphetamines. Upon arrival his vital signs and labs were found to be:

T: 98 BP: 162/92 HR: 56 RR: 16

Troponin I: 0.97a26

CK-MB: 2627

EKG: ST-depressions in anterolateral leads

The patient was started on an appropriate regimen for NSTEMI including Aspirin, Plavix, Heparin drip, Metoprolol, Nitrates, and was taken for cardiac catheterization. This study revealed no distinct vaso-atherosclerotic disease. There was noted to be TIMI II flow through the Left Anterior Descending artery (Figure 1-3).

Following administration of intracoronary nitroglycerin, TIMI 3 flow was obtained. No other Left Circumflex, Left Anterior Descending, or Right Coronary Artery lesions or flow limiting lesions were identified.



Figure 1: TIMI 2 flow through LAD.

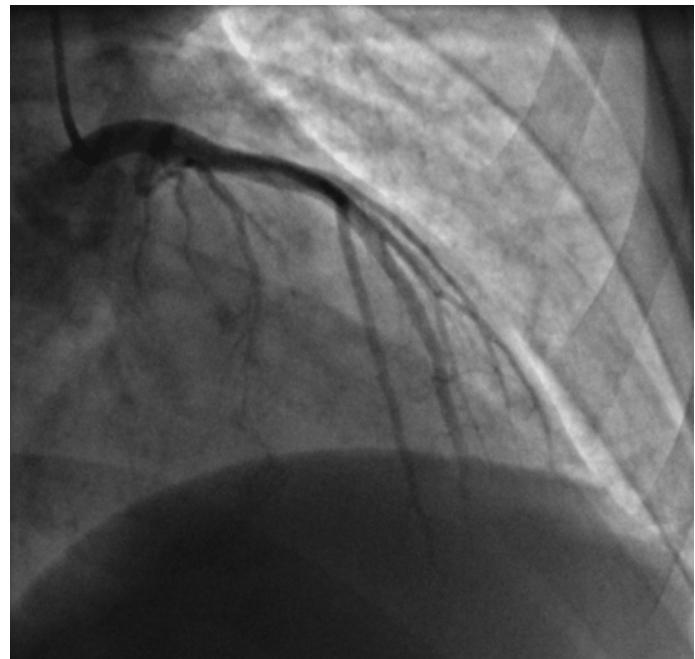


Figure 2: TIMI 3 flow following IC Nitro.

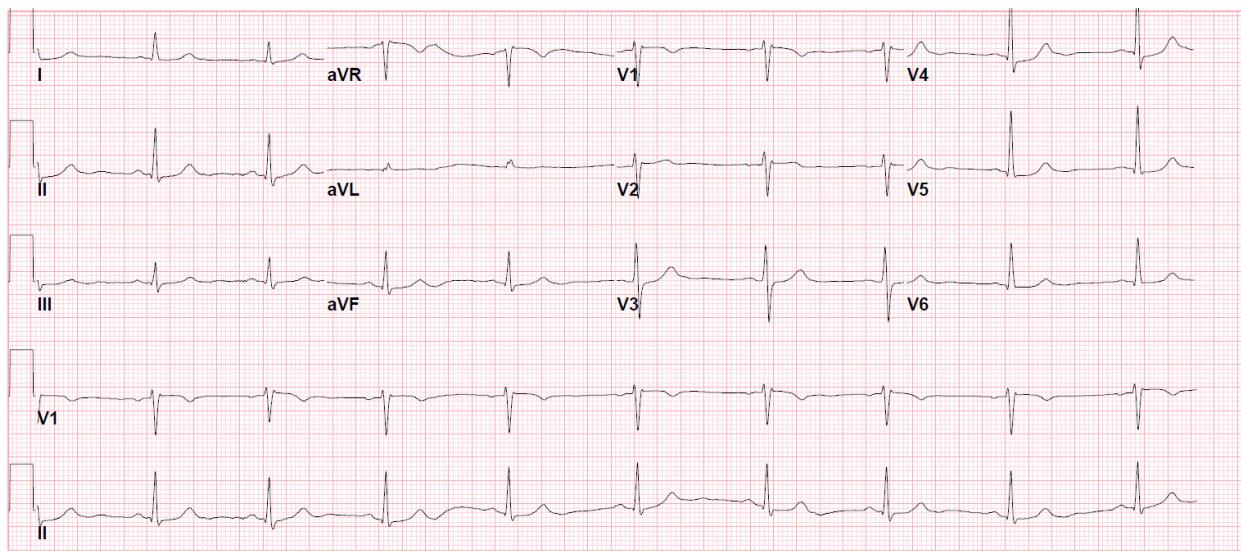


Figure 3: EKG showing ST-depressions in anterolateral leads.

Discussion

Marijuana is derived from the dried leaves of plant *Cannabis sativa*. The single most active component in Cannabis is THC (tetrahydrocannabinol) although 60 other components are also described. Because of its tendency to be more rapidly absorbed through lungs versus oral intake, it is commonly a commonly smoked substance [4]. Marijuana has a plasma half-life of 20-30 hours, hence it can be detected both in serum and urine even in occasional users [5]. It has been used for many centuries for its psychotropic effects as well as medicinal purposes in many cultures. Included among this is that the use of synthetic marijuana has been increasing during

the last decade. Many reasons exist for this but one of the main reasons is that Synthetic Cannabinoids (SC) can more difficult to detect on routine screening methods such as a standard Urine drug toxicology. DEA has identified 5 SC (JWH-018, JWH-072, JWH-200, CP-47497, {C8} CP-47497) as Level 1 controlled substances [6]. They are available by the name of K2, spice, skunk, joker and Black mamba. These can be obtained from the labs and can be used alone or in combination with other natural cannabinoids [7].

THC, the natural cannabinoid, is a partial agonist which acts on Cannabinoid receptors 1 (CB1) in the brain and on Cannabinoid Receptors 2 (CB2) located in the periphery. This produces psychotropic effects that users can experience [1]. Synthetic cannabinoids, however, are full agonists of both CB1 and CB2, and thus exert more a potent effect [8,9]. There has been active debate regarding the legislative and recreational use of marijuana. As of Jan 2018, 30 states and District of Columbia have allowed the use of marijuana in some form. Eight states along with District of Columbia have allowed the use of marijuana for recreational purposes [10]. However, prior to legalizing its use in these states, some of marijuana's potential deleterious effects have not been thoroughly explored. In 2016, WHO published an article in which the chronic use of marijuana has been associated with both serious cardiovascular and cerebrovascular events ranging from AMI to stroke [11]. The caveat was however, mentioned that stated that further research was needed to identify the underlying mechanism of these incidences. Furthermore, other cases have documented such a phenomenon of stroke secondary to marijuana use [12].

The Cardiovascular (CVS) effects of marijuana has been the topic of discussion for many years. However specifically with regards to its research, it has been challenging given the high prevalence of concurrent tobacco and other recreational drugs which are often used concurrently in those with marijuana use. Despite these challenges, the demonstration of AMI with the synthetic cannabinoid reflects the individualized side effects of cannabis [11]. E.U.I Haq et al. has have described case series which revealed individuals who utilized Spice and soon thereafter developed AMI. Two of the individuals in this case series required stent placement while one patient required aspiration thrombectomy [13]. Mehak et al. have described a case where a patient was found to have NSTEMI along with LV (left ventricle) thrombus soon after use of spice [14].

Different mechanism has been proposed for deleterious effects of cannabis on the cardiovascular system. One such case described that of a 34-year-old with inducible ventricular tachycardia on EP (Electrophysiological) studies along with reduced coronary flow presumed to be secondary to marijuana ingestion. The coro-

nary flow reverted back to normal after cessation of marijuana use [2]. Another study has hypothesized that marijuana use triggering slow coronary flow as a potential hypothesis as a mechanism of myocardial infarction [3].

It is believed that marijuana may in fact increase the risk of coronary vascular event in patients who already have coronary artery disease. A direct causation vs just correlation has not yet been established, however. The Coronary Artery Risk Development in Young Adults (CARDIA) study [15] did show that patients who used marijuana tend to have a high caloric diet and were more likely to smoke tobacco and use other illicit drugs. In 1997, Gottschalk et al. [16] published a randomized, double-blind, cross-over study of 10 patients with documented coronary artery disease. They found that smoking marijuana decreased myocardial oxygen delivery, increased myocardial oxygen demand, and decreased the time to develop angina during exercise. Marijuana smoking leads to a dose-dependent increase in carbon monoxide exposure [17] and even higher blood levels of carboxyhemoglobin than does cigarette smoking [18]. However, whether platelets play a role in marijuana-related adverse effects is currently unclear. Dahdouh et al [19] reported the case of a 20-year-old patient who abused tobacco and marijuana and developed cardiac arrest and massive myocardial infarction. Angiography showed a left main artery thrombus with no evidence of underlying atherosclerotic narrowing [19]. There is conflicting evidence regarding the effect of THC on platelets, and its role in formation of intracoronary thrombus is another area that needs further research [20].

Some potential mechanisms which have been considered for sudden cardiac death after marijuana use could be related to the development of AMI and/or arrhythmias, [21-26,27] the no-reflow phenomenon [2] or increased catecholamine levels, resulting in increased oxygen demand secondary to vasoconstriction [27,28]. Davies et al proposed that the hemodynamic effects of marijuana may cause plaque disruption, especially in the setting of a vulnerable atherosclerotic plaque, with further delineation by hemostatic and vasoconstrictive forces to form an occlusive thrombus [29]. Others have gone yet further and proposed that THC can cause necrotizing angiitis leading to thromboembolism [6,30]. Such a mechanism is supported by Disdier et al. who demonstrated the diagnosis of Buerger's disease in young male using marijuana [31].

Many times, these studies hypothesize upon mechanisms based upon limited samples, however some base their correlations upon known pathophysiological effects of cannabis on human body. One such image was documented in an article that tries to highlight and tie together these findings [32]. (Figure 4)

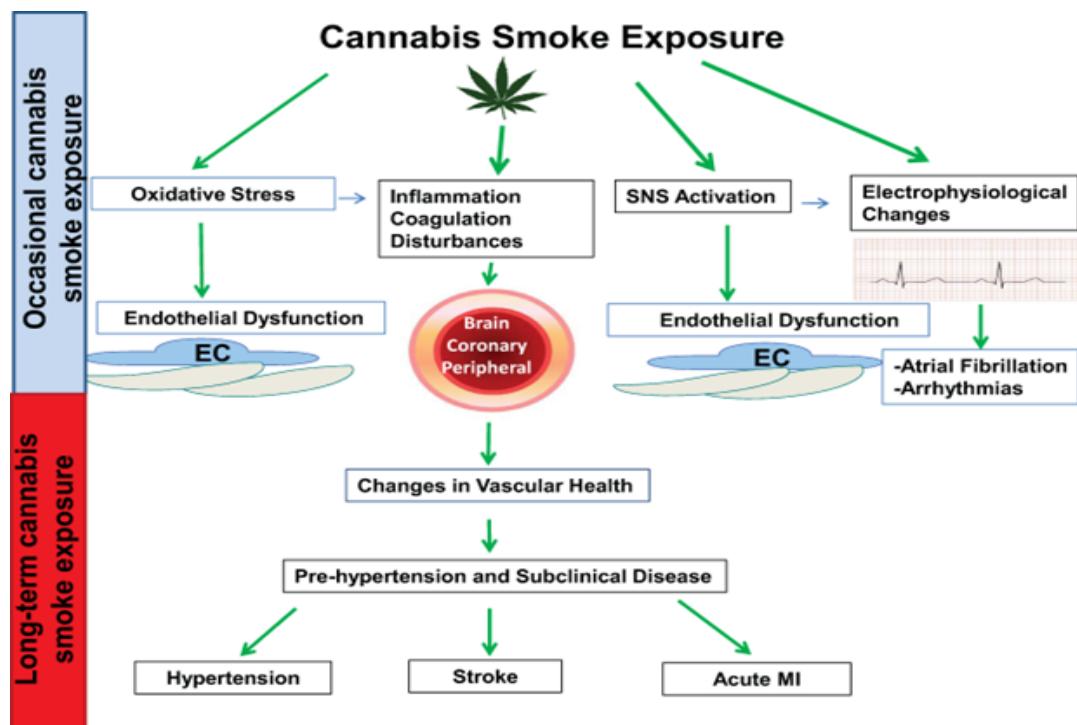


Figure 4: Although mechanisms underlying adverse CV effects of cannabis smoking are incompletely understood, several speculative mechanisms may lead to increased risk of developing certain CV conditions. EC, endothelial cells; MI, myocardial infarction; SNS, sympathetic nervous system.

Reversible vasospasm seems to be the most commonly suggested etiology for cannabis-associated acute coronary syndromes. Cardiovascular complications resulting from the consumption of marijuana have been shown to have a mortality rate of about 25% [33]. Another study showed that THC and its derivatives were reported to increase the risk of AMI by 4.8 times in the first hour after use [34]. Another showed that in marijuana consumers, the population attributable fraction for AMI was 0.8% [35]. Thus the risk between use and a very least risk of AMI appears to be moderately increased.

Such studies and evidence are not founded without prior studies on animal models. For example, there was a study on rats showed that the 1 minute second hand smoke exposure affects the endothelial vasculature for at least 90 minutes. This had a resultant effect on arterial vasodilation. This effect was considerably more potent than the similar amount of time exposure to tobacco. This study also demonstrated that second hand smoker exerts similar CVS adverse effects whether from tobacco or marijuana [36]. The various cardiovascular complications that involved marijuana as one of the culprits ranged from ventricular fib resulting in cardiac arrest [37], asystole, MI due to vasospasm alone or due to thrombosis, Pulmonary embolism, Brugada syndrome [38], LV thrombus, and various arrhythmias ranging from atrial fibrillation to ventricular tachycardia and ventricular fibrillation [39].

In 2017, Desai et al. conducted the study analyzing the lifetime odds of AMI with marijuana use and the outcomes in AMI patients with versus without marijuana use. National Inpatient Sample (NIS) database for 11-70-year-old AMI patients was analyzed. Out of 2,451,933 weighted hospitalized AMI patients, 35,771 patients with a history of marijuana and 2,416,162 patients without a history of marijuana use were identified. The AMI-marijuana group consisted more of younger, male, African American patients. The length of stay and mortality rate were lower in the AMI-marijuana group with more patients being discharged against medical advice. Multivariable analysis showed that marijuana use was a significant risk factor for AMI development when adjusted for age, sex, race (adjusted OR 1.079, 95% CI 1.065-1.093, $p<0.001$); adjusted for age, female, race, smoking, cocaine abuse (adjusted OR 1.041, 95% CI 1.027-1.054, $p<0.001$); and also when adjusted for age, female, race, payer status, smoking, cocaine abuse, amphetamine abuse and alcohol abuse. This study concluded that overall marijuana use was associated with a 3-8% increased the risk of AMI [40].

Such review of the literature reveals significant support that likelihood that marijuana, and its derivatives does have a role in development of cardiac morbidities, including development of myocardial infarction [41]. Apart from the many mechanisms described that can indirectly cause AMI, our patient was believed

to exhibit findings consistent with vasospastic etiology for his myocardial infarction. The most convincing of this etiology was the fact that his symptoms were relieved by intracoronary nitroglycerin administration. Our case is one more piece of evidence supporting that marijuana certainly has cardiotoxic effects by itself. With the growing use of marijuana in USA especially for the recreational purposes, such cardiotoxic pathologies could possibly be seen more frequently as use of marijuana rises. Such cases also highlight that clinicians should be well aware of the role of marijuana role with regards to cardiotoxicity. It also necessitates the role of further research study in exploring the direct cause and effect relationship of marijuana on AMI. We recommend further studies on the deleterious effects on marijuana should be done, and at the very least, healthcare providers and lawmakers as well have a full set of possibilities laid out prior to making further decisions which lead to a more widespread use of marijuana.

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