A case series of potential mechanisms of acute coronary syndrome in a marijuana smoker cohort

Abstract

Delta 9-Tetrahydrocannabinol (THC) is the main psychoactive component of Marijuana, a derivative of the cannabis plant. It is one of the most commonly abused mind-altering drugs in the United States (U.S). It is postulated to have thrombogenic and vasospastic potential. In this case series, we describe three patients with acute coronary syndromes and marijuana use as a common factor resulting in life-threatening outcomes mandating percutaneous coronary intervention. We highlight possible pathophysiological mechanisms underlying the effects of marijuana on coronary vasculature, making it a potential risk factor for myocardial infarction, and eventual management modalities.

Keywords: marijuana, acute coronary syndrome, percutaneous coronary intervention

Ashkan Tadayoni[1], Hira Chaudhary[1], Farla Jean-Louis[2], Ajibola Monsur Adedayo[1*], Samy I McFarlane[1], Jonathan D Marmur[1] and Erdal Cavusoglu[1]

[1]Department of Medicine, SUNY Downstate Medical Center, Brooklyn, USA

[2]Department of Medicine, Brookdale Medical Center, Brooklyn, USA

**Author for correspondence: monsur.adedayo@yahoo.com*

Introduction

Marijuana, derived from the *Cannabis sativa* and Indicia plants, is the most commonly used illicit drug in the U.S. with a prevalence of 9.5% within the adult population. The three most studied exogenous cannabinoids, the active ingredient of marijuana, are THC, cannabinol, and cannabidiol [1,2]. Cannabinoids affect the human body through the endocannabinoid system through CB1 and CB2 cannabinoid receptors. The physiological effects of THC on the cardiovascular system are mainly achieved via activation of CB1 receptors that are mainly found in the brain, heart, and lungs. Whereas CB2 receptors that, elicit a pro-inflammatory response has it distribution in lymphocytes, macrophages, and monocytes [2]. With growing recreational use, cardiovascular events related to cannabinoid have been reported. The exact causes of cardiovascular events, particularly Acute Coronary Syndrome (ACS), are not fully understood given the limited studies. We report three patients with marijuana use who developed ACS.

Patient 1

A 64-year-old male with a history of hypertension, presented with squeezing midsternal chest pain associated with diaphoresis and vomiting while smoking marijuana 30 minutes prior to admission. He admitted to daily marijuana and cigarette smoking for 20 years. No other recreational drugs and family history of cardiovascular disease.

■ Diagnostic work-up

The Electrocardiogram (ECG) showed sinus bradycardia with first degree AV block and inferior leads ST elevation. Laboratory results revealed negative troponin and Brain Natriuretic Peptide (BNP). Urine toxicology confirmed Tetra Hydro Cannabinolic Acid (THCA).

■ Intervention

He was loaded with Aspirin, Ticagrelor, and Heparin. Left Heart Catheterization (LHC) showed a 90% focal stenosis in the mid-right coronary artery (RCA) secondary to spasm that resolved after injecting intracoronary nitroglycerin with no fixed lesions **(FIGURE 1)**.

■ Outcome

The patient had no chest pain for the remainder of the hospital course. The repeat ECG showed the resolution of ST changes. Transthoracic Echocardiogram (TTE) showed inferior wall hypokinesis with the Ejection Fraction (EF) of 55%. The patient was discharged in a stable condition.

Patient 2

A 43-year-old male with a 20-year history of smoking marijuana and cigarette without any previous cardiac history presented with severe squeezing midsternal chest pain associated with dyspnea and palpitations. He denied any similar pain in the past. He had a family history of myocardial infarction in his brother and sister at ages 39 and 52, respectively.

■ Diagnostic work-up

The initial ECG showed ST elevation in V1-V4 leads. Cardiac biomarkers were mildly elevated with a troponin of 0.18 ng/mL (negative<=0.15 ng/mL) and a BNP of 167 pg/mL (negative<=100 pg/mL). Urine toxicology confirmed THCA.

■ Intervention

He was loaded with Aspirin and Plavix. The pain was persistent even though he received Tenecteplase. LHC showed a 99% obstruction in the proximal Left Anterior Descending (LAD) coronary artery and a stent was placed successfully **(FIGURE 2)**.

■ Outcome

The patient had no chest pain for the remainder of the hospital course. The following troponin peak was 0.18 ng/mL, TTE showed the EF of 40% with severe apical septal wall hypokinesis. The patient was discharged in a stable condition.

Patient 3

A 42-year-old male with a history of smoking tobacco and marijuana without any previous cardiac history, presented with substernal sharp chest pain that started 30 minutes prior to admission. The pain started suddenly at rest and was accompanied by nausea and vomiting. He denied any similar pain in the past. Last marijuana use was earlier in the morning. No other recreational drugs and family history of cardiovascular disease.

■ Diagnostic work-up

The ECG showed sinus rhythm with ST depression in V3-V4 leads. Laboratory results showed negative troponin and BNP. Urine toxicology confirmed THCA.

■ Intervention

He was loaded with Aspirin and Ticagrelor. LHC showed 100% tubular stenosis in the first Obtuse Marginal (OM1) with the filling defect consistent with thrombosis and successful balloon angioplasty was performed **(FIGURE 3)**. There was also a 100% stenosis in the mid-RCA.

■ Outcome

The patient had no chest pain for the remainder of the hospital course. The troponin increased up to 27.9 ng/ml post-cardiac catheterization, however, it down-trended appropriately. The subsequent ECG demonstrated normal sinus rhythm without any significant ST-T changes. The following TTE showed mid infero lateral wall akinesis with the EF of 61%. The patient was discharged in a stable condition.

Discussion

The distinctive common feature of this series is the cardiovascular outcome with chronic marijuana use resulting in ACS. All three patients had typical metabolites of cannabinoids detected in the urine. There are mainly three different mechanisms explored in the literature regarding the effects of cannabis on coronary vasculature i.e. platelet aggregation, atherosclerosis, and vasospasm. THC compounds are speculated to be the activator of primary hemostasis. CB1 and CB2 are the two main types of cannabinoid receptors detected on the surface of human platelets. Platelet aggregation is a dose-dependent phenomenon established with

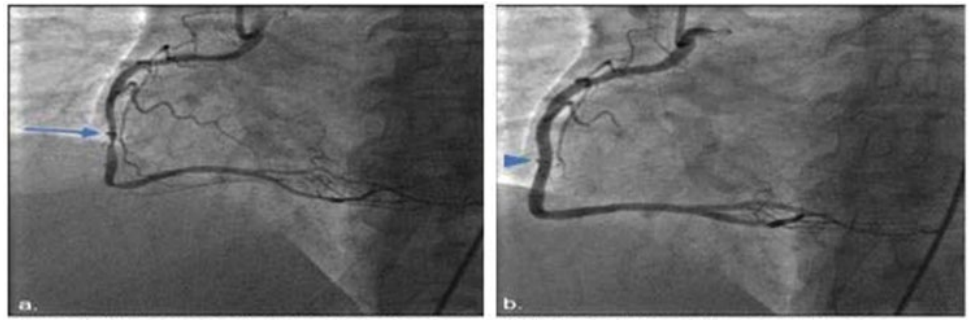

FIGURE 1. (a) Cardiac catheterization revealed mid-RCA stenosis (arrow) secondary to spasm before injecting the intracoronary nitroglycerin; (b) Cardiac catheterization revealed that the mid-RCA stenosis resolved (arrowhead) after injecting the intracoronary nitroglycerin.

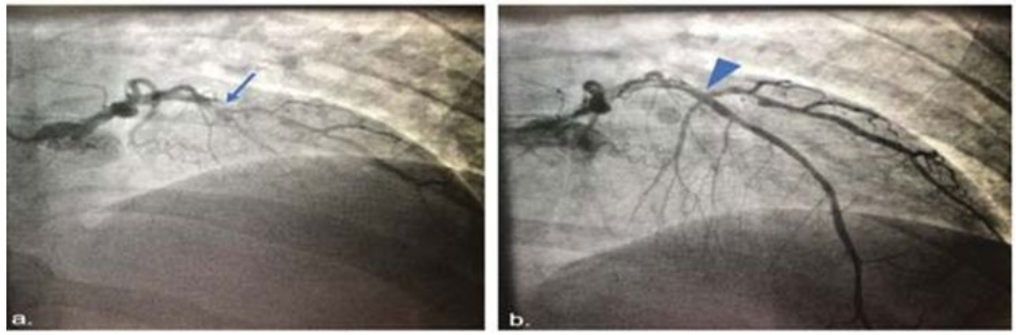

FIGURE 2. (a) Cardiac catheterization revealed a 99% obstruction in the proximal left anterior descending coronary artery (arrow); (b) Following the stent placement (arrowhead) there was an excellent angiographic appearance without any residual stenosis.

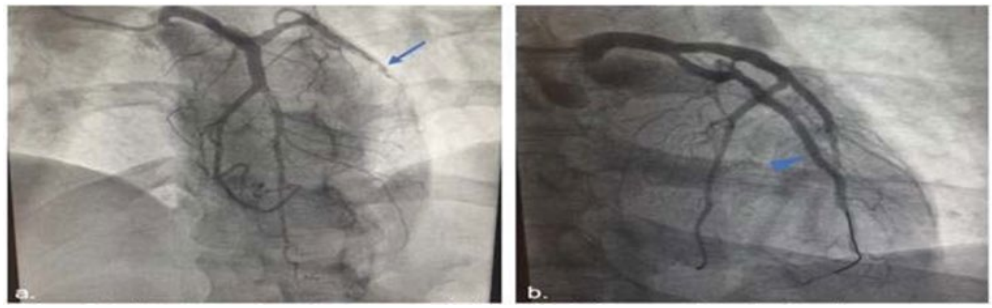

FIGURE 3. (a) Cardiac catheterization revealed 100% tubular stenosis in the 1st obtuse marginal with the filling defect; (b) Successful balloon angioplasty was performed (arrowhead).

enhanced surface expression of glycoprotein II b-III and P-selecting when treated with THC [3]. Once clotting is initiated by the extrinsic pathway of the coagulation cascade augmented by THC activated macrophages, the intrinsic pathway amplifies the response by thrombus formation and fibrin deposition [4,5]. In the third case, cannabis and tobacco smoking were the only possible risk factors for thrombus formation in the OM1 in a patient with no comorbidities.

In addition to the pro-thrombotic effects, THC causes pro-inflammatory effects by the generation of reactive oxygen species, increasing circulating catecholamine, and causing endothelial damage from oxidative stress [6]. As a consequence, disruption of a vulnerable atherosclerotic plaque is possible resulting in complete arterial occlusion [7]. CB1 receptor blockade reduced the inflammatory cytokines released from macrophages, such as interleukin-8, tumor necrosis factor-alpha, and matrix metalloproteinase-9 involved in different stages of atherosclerosis [8].

Angiographic findings in a small retrospective study of STEM I patients showed one vessel disease in marijuana users compared to non-users who had chronic atherosclerotic sequelae with two to three-vessel disease. This may imply that ischemia in such a population could be from acute thrombus formation with or without underlying atherosclerosis [9]. This explains our second case of a patient with LAD stenosis in a setting of cannabis use without any known cardiac history.

Coronary spasm is most often seen in angiographically normal arteries. In our first case, the patient had ACS secondary to coronary spasm. The defect was reversible, with the administration of intra-arterial nitroglycerin performed during angiography. However, underlying mechanisms remain unclear at this point [1]. One possible hypothesis is that ongoing cytokine release and nitric oxide from endothelial injury creates an imbalance between vasodilation and vasoconstriction. Other cardiovascular effects associated with alteration in coronary blood flow increase in resting heart rate, blood pressure, and myocardial oxygen demand as well as postural hypotension [10].

Conclusion

This case series illustrates life-threatening myocardial infarction in patients smoking marijuana. An accumulating body of evidence suggests marijuana use may be a potential risk factor for ACS with different pathways. Well-designed studies are needed to validate this association and perhaps explore the causal relationship.

References

Azofeifa A, Mattson ME, Schauer G, et al. National estimates of marijuana use and related indicators-national survey on drug use and health, United States, 2002-2014. *MMWR Surveill Summ*. 65, 1-28 (2016).

Singh A, Saluja S, Kumar A, et al. Cardiovascular complications of marijuana and related substances: a review. *Cardiol Ther*. 7, 45-59 (2018).

Deusch E, Kress HG, Kraft B, Kozek-Langenecker SA. The procoagulatory effects of delta-9-tetrahydrocannabinol in human platelets. *Anesth Analg*. 99, 1127-1130 (2004).

Williams JC, Klein TW, Goldberger BA, et al. Δ(9)-Tetra Hydro Cannabinol (THC) enhances lipo polysaccharide-stimulated tissue factor in human monocytes and monocyte-derived microvesicles. *J Inflamm (Lond)*. 12, 39 (2015).

Mackman N, Tilley RE, Key NS. Role of the extrinsic pathway of blood coagulation in hemostasis and thrombosis. *Arterioscler Thromb Vasc Biol*. 27, 1687-1693 (2007).

Subramaniam VN, Menezes AR, De Schutter A, Lavie CJ. The cardiovascular effects of marijuana: are the potential adverse effects worth the high? *Mo Med*. 116, 146-153 (2019).

Johnson S, Domino EF. Some cardiovascular effects of marihuana smoking in normal volunteers. *Clin Pharmacol Ther*. 12, 762-768 (1971).

Sugamura K, Sugiyama S, Nozaki T, et al. Activated endocannabinoid system in coronary artery disease and anti inflammatory effects of cannabinoid 1 receptor blockade on macrophages. *Circulation*. 119, 28-36 (2009).

Lee J, Sharma N, Aponte CS, et al. Clinical characteristics and angiographic findings of myocardial infarction among marijuana users and non-users. *Scifed J Cardiol*. 1, 1000008 (2017).

Mittleman MA, Lewis RA, Maclure M, Sherwood JB, Muller JE. Triggering myocardial infarction by marijuana. *Circulation*. 103, 2805-2809 (2001).