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Myocardial Infarction Secondary to Marijuana-Induced Coronary Vasospasm

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Abstract With the rise of the number of states fully legalizing marijuana, the use of this substance in the United States is at an all-time high. This increasing legalization gives the impression that marijuana is rather safe. However, multiple reports by our groups and others documented serious cardiovascular complications associated with marijuana use ranging from life threatening arrhythmia to myocarditis and myocardial infarction. In this report, we present a case of a 61 year old man presented with left sided typical chest pain shortly after marijuana consumption with the diagnosis of non ST-elevation myocardial infarction (NSTEMI) established based on clinical, EKG and troponin values with eventual cardiac catheterization documenting non-occlusive coronary artery disease with 30% obstruction of the proximal first obtuse marginal artery. We also review the putative pathophysiologic mechanisms of marijuana induced coronary vasospasms, highlighting the implications of these findings in the evaluation and management of cardiac chest pain in marijuana users.

Keywords: *marijuana, cannabis, myocardial infarction, vasospasm*

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1. Introduction

With the recent increase in legalization of recreational and medical marijuana across the United States over the past decade, clinicians have seen a dramatic rise in marijuana related hospitalizations. With Colorado being the first state to legalize recreational marijuana (cannabis) it has become the center of a nationwide study demonstrating the effects increased marijuana consumption has on hospitalizations. A recent 2016 study conducted by Colorado Health Department, showed that since the passing of recreational marijuana use there has been a staggering increase in hospitalizations secondary to marijuana use (Figure 1) [1]. We present a case of non-ST segment myocardial infarction secondary to marijuana induced coronary vasospasm (prinzmetal angina) in an elderly male who presented with chest pain after recreational marijuana use.

Endocannabinoids have multiple effects on various organs/organ systems primarily though transmembrane receptors that are G-protein coupled- CB1 and CB2. CB1 is known for its inflammatory role, and conversely CB2 having anti-inflammatory properties [2,3,4]. It has been shown through molecular biological analysis via western blot and flow cytometry that CB1 receptors are expressed within the endothelium [4]. CB1 receptors activation within the coronary endothelium amplifies the reactive oxygen species-mitogen-activated protein kinases (ROS-MAPK) activation cell death pathway leading to excessive inflammation and oxidative stress formation causing endothelial dysfunction [3,4]. ROS can trigger vasoconstrictor stimulus, in addition to the direct G-protein and ion channel dysregulation with CB1 activation which both combined leads to smooth muscle cell hyper reactivity within coronary vessels [2,3,4].

2. Case Report

A 61-year-old man with a history of vasospastic angina, hyperlipidemia, asthma, and implantable cardioverter-defibrillator as he had survived ventricular tachycardia (secondary prevention), presented with sharp substernal chest pain that radiated down the left arm, 10/10 in intensity. He also complained of associated nausea, and had experienced a one-time episode of non-bloody, non-bilious vomiting, along with diaphoresis. At presentation his pulse was 89 beats per minute and

blood pressure was 148/72 mm Hg. Electrocardiogram (EKG) showed tall hyper acute T-waves in the precordial leads V2-V4 (Figure 1). Chest x-ray was negative for any intrapulmonary pathologies, and BNP was 73 pg/ml. Initial troponin was 0.17 mg/dl, which trended up to 0.19, 0.40 and peaked at 0.69 mg/dl. Of note, the patient had initially denied taking any illicit drugs, it was not until later that the patient stated that it was his birthday and he had smoked marijuana earlier that day and shortly before experiencing chest pain. Upon evaluation in the emergency department, he stated that his symptoms began to slightly improve with one-time sublingual nitroglycerin. A diagnosis of non ST-segment myocardial infarction was established (NSTEMI) and aspirin 325 mg, clopidegrol 300 mg and heparin drip were initiated as a part of NSTEMI management protocol. Patient underwent urgent coronary angiogram which revealed minimal coronary irregularities suggestive of non-obstructive CAD and 30% obstruction of the proximal first obtuse marginal artery was noted (Image 1 and Image 2). When compared with his angiogram from another hospital of 2018, there were no changes in the coronaries. No acute occlusions, stenosis, or changes were noted when compared to the patients' previous angiogram from the previous year. Upon through review of reports his previous hospitalization at other facilities it became apparent that patient had similar presentations with chest pain after smoking marijuana and was managed medically for NSTEMI and coronary angiogram had not shown any flow limiting stenosis. Patient was educated on stopping smoking in general, but specifically refraining from marijuana use to which he agreed. Patient was discharged on dual antiplatelet therapy, calcium channel blocker diltiazem and high intensity statins. Beta-blockers were not prescribed as patients

3. Discussion

Our diagnosis of vasospastic angina was made based on the Coronary Vasomotion Disoders International Study group (COVADIS) criteria [5]. The criteria states that there should be nitrate responsive angina with an associated transient EKG changes. Angiographic evidence of coronary evidence of coronary artery spasm is not required but can be replaced with EKG findings. A provocation test of coronary spasm and subsequent response with nitrates and/or CCB was not done in this patient. With the temporal association of his marijuana use and subsequent vasospastic angina pain, marijuana was suspected to be the primary trigger in his case.

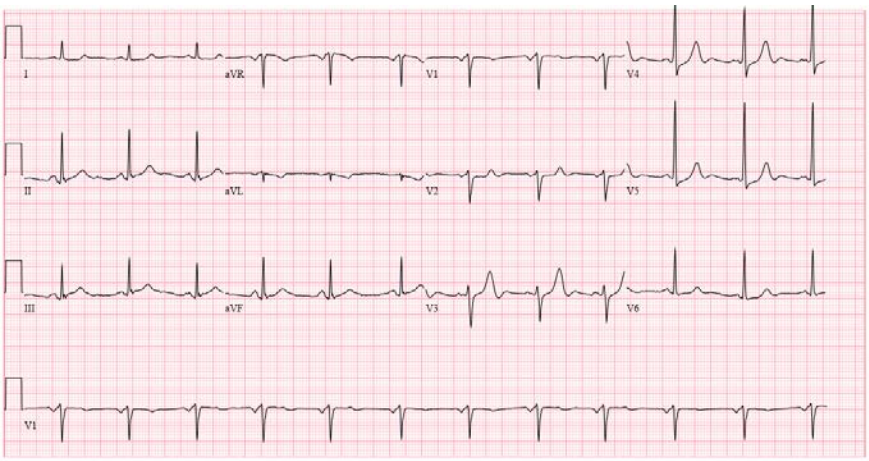

Figure 1. EKG showing tall hyper acute T-waves in the precordial leads V2-V4. NSR

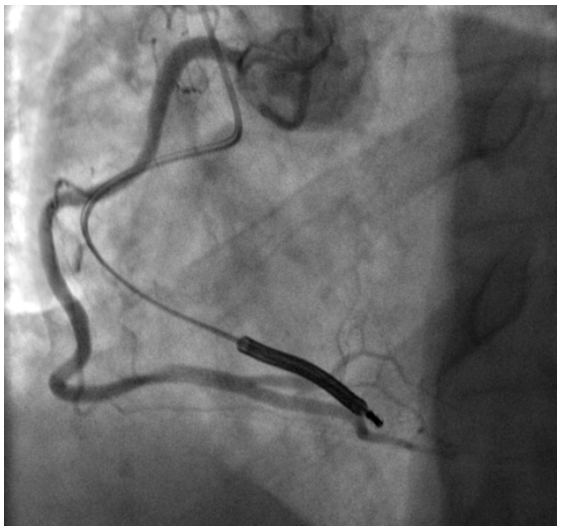

Image 1. Right coronary artery angiogram in left anterior oblique caudal view showing mild luminal irregularities and no obstructive lesion.

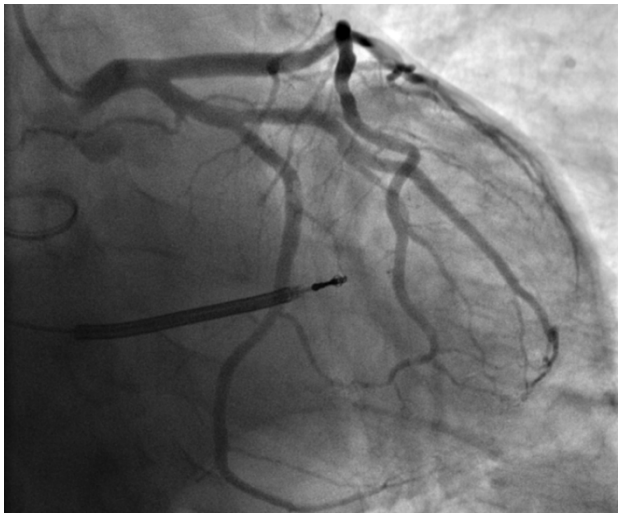

Image 2. Left coronary artery angiogram in right anterior oblique caudal view showing mild luminal irregularities and no obstructive lesion

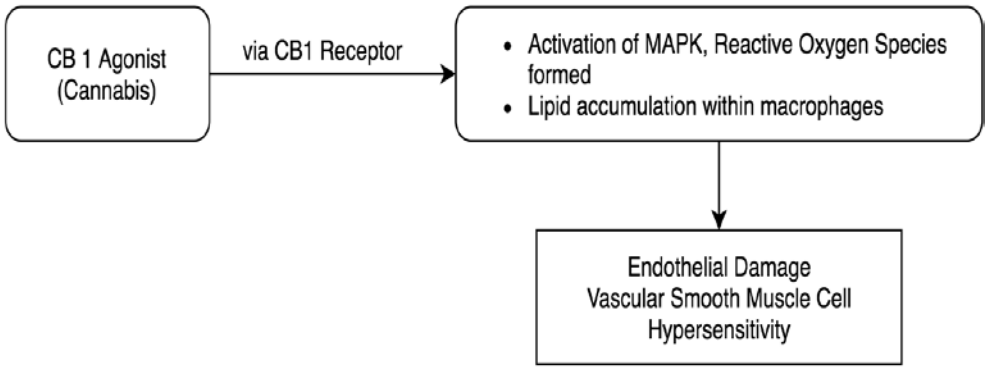

Figure 2. Proposed Pathogenetic mechanisms of Endothelial Damage associated with cannabis use

There are numerous pathophysiology mechanisms by which marijuana can cause myocardial infarction [6]. The endothelium plays an important role in the regulation of the coronary vascular tone [7,8,9]. This is primarily done with the help of several vasodilators, the most important of which is nitric oxide (NO) released by coronary endothelial cells [8]. Hence, endothelial damage can impair vasodilation, favoring coronary artery spasms (CAS) in response to a vasoconstrictor stimulus (Figure 2) [4,7]. It is known that marijuana activates CB1 receptors within the endothelium and there is a ROS-MAPK activation cascade [4]. This results in the generation of multiple ROS, which is a vasoconstrictive stimulus leading to smooth muscle constriction within coronary vessels [6]. Of note, not only are ROS a vasoactive stimulus but they also promote endothelial damage, starting the pathogenesis in the first place [4,6] Multiple cases of coronary slow and no flow phenomenon has been reported [10,11,12]. Coronary Slow Flow Phenomenon (CSFP) is an angiographic finding, where by there is a delay in distal vessel opacification in the absence of a significant occlusion and/or stenosis of the coronary vessel [13]. This underlying innocuous finding has great clinical implications since it has been linked to various effects such as myocardial ischemia, recurrent ACS, arrhythmias, and even sudden cardiac death [14-18]. In addition, CSFP and vasospastic angina share common features, such as both improve symptomatically from chest pain following oral calcium channel blockers (CCB) an oral nitroglycerin [15]. Individuals who were observed with CSFP and had endomyocardial biopsies were observed to have fibromuscular hyperplasia, endothelial degradation, reduction in lumen size, and abnormalities of the mitochondria, and glycogen content [6]. It is likely based on these findings that CSFP is multifactorial, altering the endothelium on a biochemistry level. Coronary angiograms in these patients with CSFP are classically referred to as “negative and normal,” or to have “minimal non-obstructive disease,” which leads to patients being referred to as negative cardiac catheterization myocardial infarctions [19,20]. These findings correlate with what was seen objectively within our case report. There are documented cases which associate CSFP with marijuana use, in addition there have been correlation of CSFP and runs of ventricular tachycardia as well [19]. Finally, when marijuana induced myocardial infarction is secondary to vasospasm the appropriate management would be abstinence to marijuana, dual antiplatelets, high intensity statins and calcium channel blockers as well as nitrates [21].

4. Conclusion

In this report, we presented a unique case of myocardial infarction, induced by coronary vasospasm associated with marijuana use. While cardiovascular complications associated with marijuana use are published by multiple authors, including several papers from our group, vasospastic coronary angina, that is commonly reported with cocaine abuse, has not been sufficiently emphasized in the literature. This fact in and of itself gives our current case report the novelty as well as the impotence to highlight this critical association between coronary vasospasm and marijuana that is currently the most commonly abused recreational drug in the USA.

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