

Marijuana and Coronary Dissection: A Case Report and Review of Literature

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Abstract Spontaneous coronary artery dissection (SCAD) is a cardiac emergency and an uncommon cause of acute coronary syndrome (ACS) with a higher predominance in younger women. It is a non-traumatic, non-atherosclerotic lesion found to be associated with pregnancy, inflammatory disorders, connective tissue diseases and substance abuse. Our patient was a young woman with a chronic marijuana smoking history who was found to have a NSTEMI. Initial angiogram showed triple vessel disease involving left anterior descending artery (LAD), left circumflex artery (LCX) and obtuse marginal artery (OM). A repeat angiogram notably showed spontaneous progression with dissection in all three vessels attributable to substance abuse. We present you this rare occurrence of triple vessel SCAD secondary to marijuana with a literature review and discussion.

Keywords: *marijuana, coronary artery dissection, risk factors*

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1. Introduction

Coronary artery dissection is an uncommon emergency condition that occurs when a tear forms in a blood vessel in the heart and can occur secondary to atherosclerosis, instrumentation, mechanical trauma, arrhythmias or spontaneously. Spontaneous dissection in a patient with no prior cardiac history is a rare cause of acute coronary syndrome (ACS) and carries the potential of deterioration into sudden cardiac death. Spontaneous coronary artery dissection (SCAD) is defined as non-traumatic, non-iatrogenic, non-atherosclerotic separation of the coronary arterial wall leading to the formation of a false lumen with or without an intimal tear. This separation may occur between the intima and media or the media and adventitia leading to the formation of an intramural hematoma (IMH) within the walls. The IMH rather than atherosclerotic plaque rupture or intraluminal thrombus can obliterate the lumen of the coronary artery reducing anterograde blood flow leading to myocardial ischemia or infarction [1,2]. The true incidence of SCAD is unclear

predominantly because it remains underdiagnosed. Studies report an incidence of 1.1% - 4% all ACS cases as being secondary to SCAD with the majority of cases seen predominantly affecting women [3,4]. SCAD has been associated with pregnancy, fibromuscular dysplasia, multiparity, systemic inflammatory disease and connective tissue disorders [5,6,7,8,9].

Although the spectrum of presentation of SCAD may vary depending on the extent of blood flow limitation, patients typically present with angina or its equivalents, ischemic ECG changes and elevation of cardiac biomarkers [5,10]. Based on their presentation of ACS these patients often undergo coronary angiography which demonstrates obliteration of the lumen of the coronary artery by the IMH. Comprehensive evaluation of the IMH is often then assessed with the use of intravascular ultrasound (IVUS) and optical coherence tomography (OCT). Cardiac CT angiography has emerged as a useful modality to subsequently monitor arterial healing in patients with SCAD.

Few scattered cases of SCAD have also been reported with the use of recreational drugs like cocaine [11], methamphetamine [12] and marijuana [13,14,15,16,17].

Marijuana has been implicated as causative in a wide spectrum of cardiac disorders which range from ACS, coronary spasm, myocarditis to arrhythmias [18,19,20,21,22,23]. However, the presentation of SCAD with marijuana has rarely been reported. We are reporting a rare case of SCAD occurring secondary to chronic marijuana use in a young female patient. Our literature review yielded only 6 cases of SCAD with marijuana use. Our case is also only the second ever reported case of a triple vessel SCAD with marijuana [14].

2. Case Report

A 25-year-old African-American female presented to the emergency room with 2 hours of aching left-sided, 7/10 intensity, non-radiating non-pleuritic chest pain. The pain had been associated with shortness of breath, nausea and 1 episode of non-bloody non-bilious vomiting. She had been a regular marijuana smoker since the age of 15. She smoked one blunt each day after work and two blunts on the weekend. She was not on any oral contraceptive pills and only used an over-the-counter multivitamin syrup. She had been in good health prior to the onset of symptoms and had a good exercise tolerance. Her heart rate was 81 beats/minute, respiratory rate 18 cycles/minute, 106/56 mm of Hg, saturation 98% on room air and was afebrile. Her physical exam was unremarkable. She had no jugular venous distention or pedal edema. Her chest was bilaterally clear to auscultation. First and second heart sounds were appreciated and no murmurs were auscultated. ECG was consistent with a normal sinus rhythm and incomplete right bundle branch block pattern (QRS duration 108 msec.). A complete blood count, comprehensive metabolic panel, D-dimer and lipid panel were within normal limits. The initial troponin at presentation was 2.9 ng/ml, which subsequently peaked at 7.5 ng/ml 12 hours later. A diagnosis of non-ST segment elevation myocardial

infarction was established. Her pain resolved completely in the emergency room with the administration of sublingual nitrate. She was treated with 325 mg of Aspirin, 300 mg of Clopidogrel and 1mg/kg of enoxaparin and referred for cardiac catheterization. Right femoral arterial access was obtained and a 6F sheath was introduced. Right radial access had failed due to radial artery spasm. Right coronary angiography was performed with a 6 French three-dimensional right curve (3DRC) catheter. Dissection of the proximal right coronary artery with closure of the posterior descending artery was appreciated (Image 1); Left coronary artery collaterals to the right coronary distribution were appreciated (Image 2). The patient was asymptomatic and hemodynamically stable at this time and no EKG changes were observed. A 6 French JL4 catheter was used to engage the left coronary system which revealed diffuse 60% narrowing of the proximal left anterior descending artery and focal 70% stenosis of the distal circumflex before the origin of the third obtuse marginal artery (Image 3). Ventriculography established a left ventricular ejection fraction of approximately 55%. A diagnosis of triple vessel coronary artery disease was established and she was referred to a tertiary care center for coronary artery bypass grafting. At the referral center the patient developed symptomatic hypotension and a decision was made to perform a repeat coronary angiogram. A repeat angiogram of left coronary artery showed diffuse 80-90% long narrowing of the proximal left anterior descending artery. This was more severe than 60% narrowing noted in the initial angiogram thus a diagnosis of dissection was established. There was also a diffuse 70% narrowing of the left circumflex artery (blue arrow) and appearance of subtotal occlusion of the obtuse marginal artery suggesting both the lesions in left circumflex artery and obtuse marginal artery to be dissection. (Image 4, Image 5). She was transferred to a heart transplant center for left ventricular assist device placement as a bridge to cardiac transplant.



Image 1. Left anterior oblique caudal view of the right coronary artery in which dissection is evident

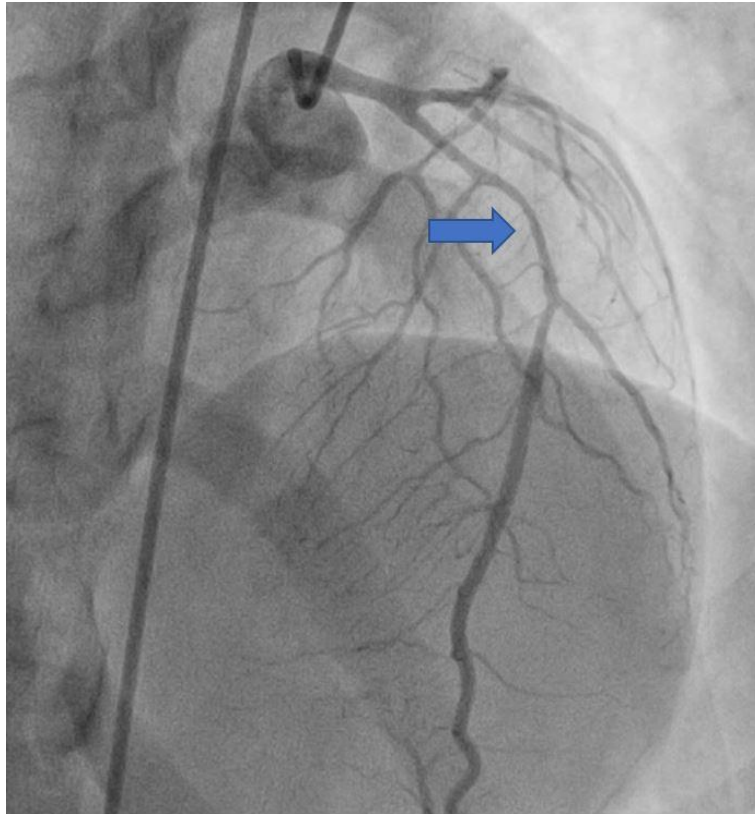


Image 2. Right anterior oblique cranial view of the left coronary artery showing diffuse 60% narrowing of the proximal left anterior descending artery

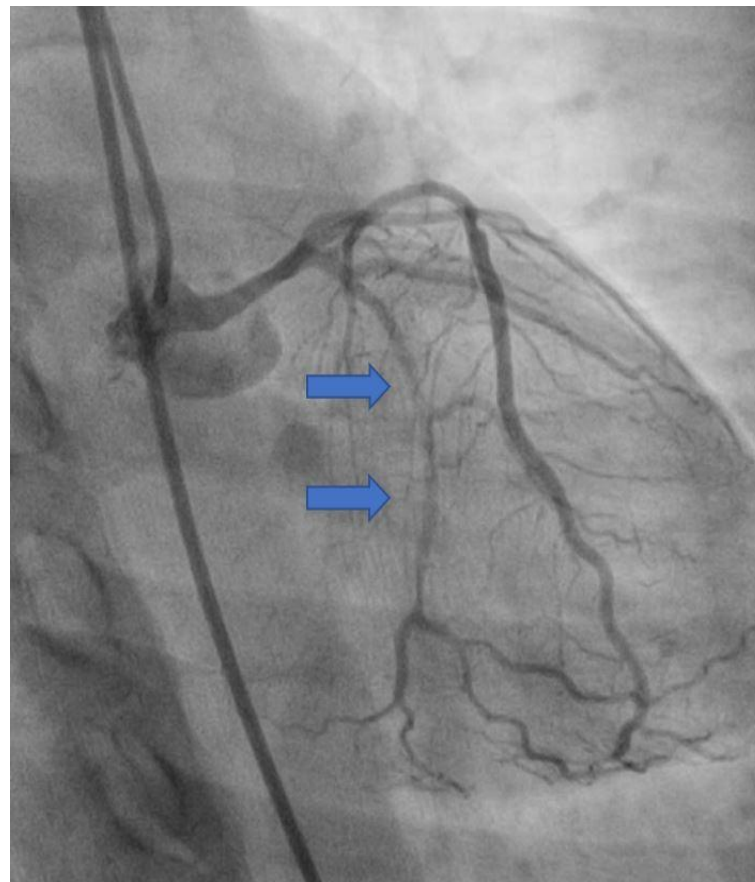


Image 3. Right anterior oblique cranial view of the left coronary artery showing diffuse 70% narrowing of the left circumflex artery

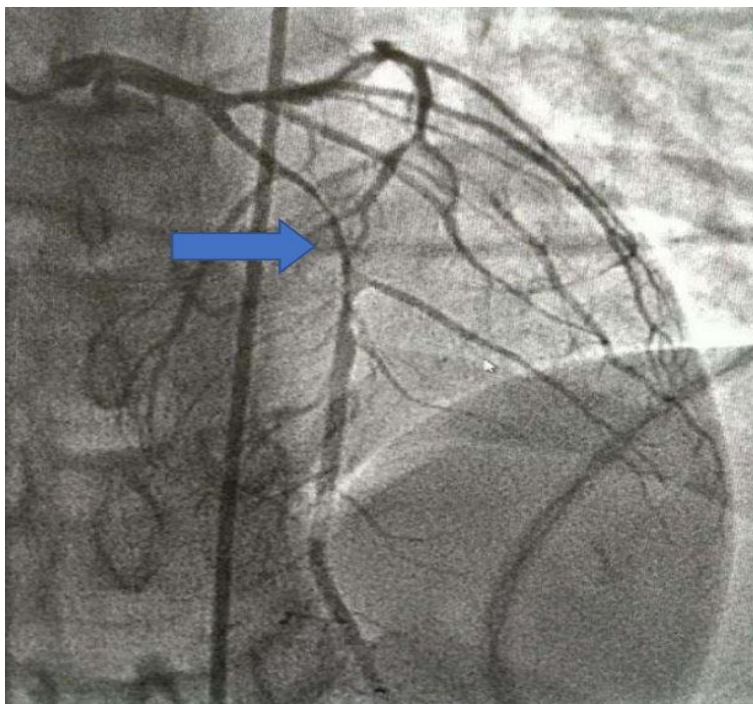


Image 4. A repeat angiogram in the right anterior oblique cranial view of the left coronary artery showing diffuse 80-90% long narrowing of the proximal left anterior descending artery. This was more severe than 60% narrowing noted in the initial angiogram thus a diagnosis of dissection was established

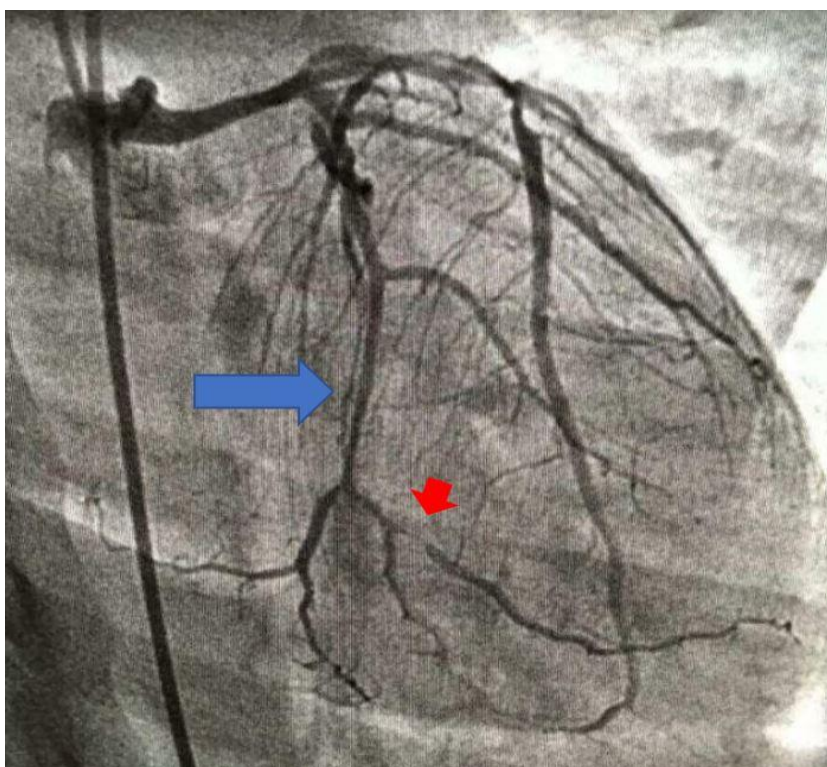


Image 5. A repeat angiogram in the right anterior oblique cranial view of the left coronary artery showing improvement in the diffuse 70% narrowing of the left circumflex artery (blue arrow) also appearance of subtotal occlusion of the obtuse marginal artery was noted suggesting both the lesions in left circumflex artery and obtuse marginal artery to be dissection

3. Discussion

The underlying mechanism of non-atherosclerotic SCAD is not fully understood, but an intimal tear or bleeding of vasa vasorum with intramedial hemorrhage has been proposed. Both result in creation of a false lumen filled with intramural hematoma [24,25]. SCAD is a

disease which predominantly affects women (>90% of all documented cases). It has been estimated to be the etiology of 15%-35% of all cases of ACS in women presenting under the age of 50 [26,27,28]. Studies also show that women account for 81-100% of cases of SCAD in the age range of 45-56 years [6,7,29,30,31]. SCAD has been most notably associated with pregnancy, with 40%

of myocardial infarctions during pregnancy being secondary to SCAD. Multiparity, fibromuscular dysplasia owing to associated coronary artery tortuosity, systemic lupus erythematosus, connective tissue disorders like Marfans' syndrome, Ehlers Danlos syndrome and Takotsubo cardiomyopathy are conditions which predispose to SCAD. A review of 20,195 patients with ACS from Japan revealed prevalence of SCAD in 0.31% (females 94%) with 29% developing after emotional stress. Other triggers for SCAD other than emotional stress include physical exertion, Valsalva-like maneuvers, corticosteroids use and recreational drugs abuse (cocaine, methamphetamine and marijuana) [6,7,8,9,32,33,34].

Tetrahydrocannabinol (THC) is the active component in marijuana and binds to the CB1 and CB2 receptors. Activation of receptors in the cardiovascular system increases sympathetic stimulation leading to tachycardia, peripheral vasodilation, elevated systolic and diastolic blood pressures and augmentation of left ventricular function [35,36,37]. THC also increases the risk of ACS 4.8 times within the 1st hour of its use, has a procoagulant effect and a tendency to provoke cardiac arrhythmias [38]. The mechanism behind marijuana use leading to SCAD is not completely understood. Sympathetic overdrive and elevated blood pressures likely lead to an increased shear stress on the coronary arterial wall leading to SCAD in susceptible individuals.

While most patients with SCAD have a presentation similar to ACS, a small proportion of patients present with syncope, ventricular arrhythmias and cardiogenic shock [10,31]. There is often a reversible drop in ejection fraction which may show improvement after revascularization [39]. Anatomically the left anterior descending artery is most commonly culprit vessel followed by circumflex and right coronary arteries [30]. Single vessel dissection is the most common presentation, but 9-19% of cases have multivessel involvement [28,30]. While dissections predominantly affect the mid to distal segments of coronaries, <10% affect the proximal segments [7]. Triple vessel SCAD though extremely rare has been reported [14,40].

Angiographically SCAD may demonstrate extraluminal contrast staining, multiple radiolucent lumens, spiral dissection or intraluminal filling defects [41]. On occasion it may mimic atherosclerosis and give the appearance of diffuse or focal tubular stenosis [25]. While conventional angiography helps visualize the lumen of the coronary arteries it does not image the arterial wall. This limits its utility in SCAD which is predominantly an intramural pathology of the coronary arterial walls. Intracoronary

imaging techniques like optical coherence tomography (OCT) and intravascular ultrasound (IVUS) provide much more data on the composition of the vessel wall and aid in visualizing the false lumen, intimal tear and hematoma when present. Instrumentation induced vessel wall injury should always be considered while performing intracoronary imaging. OCT has been demonstrated to be superior to IVUS in terms of providing better spatial resolution and finer depiction of vessel wall [42].

There have been no randomized controlled trials to guide the management of SCAD. While conservative management can be attempted in hemodynamically stable patients without ongoing chest pain, patients with ongoing chest pain, dynamic ECG changes or hemodynamic instability are often taken to the cardiac catheterization suite for percutaneous intervention [7]. Affected coronary arteries are often weak, rendering them susceptible to iatrogenic dissections through intubation of the false lumen [5,26,29,43]. An individualized decision taking into consideration the risks and benefits of the intervention should be made for each patient. CABG is the preferred treatment strategy in patients with SCAD of left main coronary artery, proximal dissections, patients in whom primary PCI has failed or when the lesion is not anatomically suitable for PCI [44]. While beta blockers, angiotensin converting enzyme inhibitors or angiotensin receptors inhibitors, dual antiplatelet therapy and heparin are routinely administered, the role of GPIIb/IIIa inhibitors and thrombolytic in this population has never been prospectively studied. Multidetector cardiac CT imaging is now being increasingly used to follow the course arterial healing after SCAD in those with proximal large caliber arteries [45]

A comprehensive review of existing literature shows that the incidence of SCAD in the setting of marijuana use has been rarely reported. There have been only 7 reported cases till date including ours.

In our review, we found that these patients were fairly young with a mean age of 30 (Table 1 & Table 2). Interestingly 71% of the patients were male. None of these patients had any cardiovascular risk factors of obesity, diabetes, hyperlipidemia, hypertension, chronic kidney disease or a family history of coronary artery disease. Almost unanimously all the cases presented with typical ACS like pictures with chest pain, ECG changes and elevated cardiac bio markers. The most commonly affected artery was proximal LAD (Table 3) [13,14,15,16,17]. Our review yielded only one case with triple vessel involvement [14]. 2 of the patients underwent drug eluting stent and 1 underwent CABG [14,15,16].

Table 1. Reported cases of coronary dissection secondary to marijuana use

Year of publication and Author	Country	Artery affected	Number of results affected
2011, Schmid (13)	Austria	Proximal LAD	1
2013, Filali (14)	Tunisia	Proximal LAD, LCx, RCA	3
2015, Tariq (15)	USA	Proximal LAD, diagonal 1	2
2015, Cruff (16 Obesity 0 Diabetes 0 Hyperlipidemia 0 Hypertension 0 Chronic kidney disease 0 Family history of coronary artery disease 0)	USA	Proximal LAD	1
2016, Noamen (17)	Tunisia	Proximal LAD	1
2016, Noamen (17)	Tunisia	Proximal LAD	1
2019, Theetha Kariyanna (present case)	USA	Proximal LAD, proximal RCA, mid- LCx	3

Table 2. Summary of Patient Characteristics

Total number of cases	7
Cases reported from	USA 3 (43%) Tunisia 3 (43%) Austria 1 (14%)
Age	Median = 27 ± 6.5 years Mean = 30 ± 6.5 years
Sex	Male 5 (71%) Female 2 (29%)
Presenting symptoms	Chest pain 7 (100%)
Other drug use	History of heroin use 1 (14%) History of cocaine use 1 (14%)
History of smoking	3 (43%)
Other cardiovascular risk factors reported	Obesity 0 Diabetes 0 Hyperlipidemia 0 Hypertension 0 Chronic kidney disease 0 Family history of coronary artery disease 0
Reported ECG finding	STEMI 4 (57%) Dynamic ST segment changes 1 (14%) Incomplete RBBB 1 (14%) Poor R wave progression 1 (14%) Reported arrhythmias 0 (0%)
Imaging studies	Wall motion abnormality on echocardiography reported in 5 (71%) Normal EF was reported in 4 (57%)
Management	Underwent DES 2 (29%) Referred for CABG 1(14%) Referred for cardiac transplant 1 (14%)
Reported death	1 (14%)

CABG: coronary artery bypass graft **DES:** drug-eluting stent **ECG:** electrocardiogram **EF:** ejection fraction **RBBB:** right bundle-branch block, **STEMI:** ST segment elevation myocardial infarction.

Table 3. Summary of coronary angiogram and management

Publication Year/author	Coronary Artery affected	Coronary angiogram findings	Intravascular ultrasound	Medical management	Invasive management	Death
2011, Schmid [13]	Proximal LAD	pLAD dissection	-	Dual antiplatelets, B-blockers, ACEi		-
2013, Filali [14]	Proximal LAD, LCx, RCA	Luminal narrowing of pLAD. Dissection of LAD extending into second segment without flow limitation, dissection in proximal Cx and mid RCA	-		Coronary artery bypass surgery	Yes
2015, Tariq [15]	Proximal LAD, diagonal 1	pLDA dissection 90% obstruction, occlusion of D1	Proximal LAD dissection	GDMT	Drug-eluting stent to both vessels	-
2015, Cruff [16]	Proximal LAD	pLAD dissection	-	Aspirin, B- blockers, LMWH	DES placement	-
2016, Noamen [17]	Proximal LAD	pLAD dissection	Proximal LAD dissection	Tirofiban		-
2016, Noamen [17]	Proximal LAD	pLAD dissection	Proximal LAD dissection	Tirofiban		-
2019, Theetha Kariyanna (present case)	Proximal LAD, proximal RCA, mid- LCx	pLAD dissection, proximal RCA dissection, mid Cx dissection		Dual antiplatelets LMWH B-blockers Statins	Referred for cardiac transplant	-

ACEi: angiotensin-converting enzyme inhibitors **Cx:** circumflex artery **DES:** Drug-eluting stent **D1:** first diagonal artery **GDMT:** goal directed medical therapy **LDA:** left anterior descending **RCA:** right coronary artery, **LMWH:** low molecular weight heparin **pLDA:** proximal left anterior descending artery.

4. Conclusion

Our case represents only the 7th reported case of SCAD with Marijuana use and the 2nd such case with triple vessel

involvement. The legalization of recreational marijuana in many states across the United States has led to a surge in its use especially among the younger generation. Our study aims to alert the physicians to consider SCAD in the

differential of an otherwise healthy young patient presenting with symptoms of ACS.

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