Cannabis-induced basal-mid-left ventricular stress cardiomyopathy: A case report

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ABSTRACT
Cannabis, popularly known as marijuana, is a recreational drug derived from the plant Cannabis Sativa. It has been recognized as the most widely used mood-altering substance in the world and is falsely perceived as a safe substance by the public at large. This is mostly due to lack of awareness of its adverse effects as well as successful attempts for legalization of its use in many states. We present a unique case of a 56-year-old man who presented with neurological deficits concerning for stroke. Soon after presentation, he required endotracheal intubation for airway protection due to worsening mental status changes and pulmonary edema. Echocardiogram revealed severe hypokinesis of the basal and mid-left ventricular (LV) walls with hyperdynamic motion of the apex (reverse takotsubo). Coronary angiography revealed no obstructive disease. Urine toxicology screen was positive for Δ9-tetrahydrocannabinol. The patient then stated to have used excess marijuana before the symptom onset, while denying any recent emotional stressors. The findings were consistent with stress cardiomyopathy (SC) triggered by marijuana use. Myocardial infarction, stroke, and peripheral arteriopathy have been increasingly reported in younger individuals using marijuana. SC appears to be another unique complication of marijuana use triggered through its effects on the autonomic nervous and endocannabinoid systems.

Key Words: Cannabis, left ventricular regional ballooning, marijuana, stress cardiomyopathy, takotsubo

INTRODUCTION
Based on the 2016 World Drug Report, cannabis is the most widely used recreational substance and nearly 3.8% of the world population use it annually.[1] The prevalence of cannabis dependence was estimated at 13.2 million individuals worldwide in 2010[2] with a tremendous rise in recreational cannabis use in parallel with legalization of its possession and use as well as cultivation of the plant.[3] Recently, an increasing number of case reports have been published in regards to serious cardiovascular complications occurring in younger individuals in temporal relation to recreational cannabis use.[4] Most prominently among these complications have been acute coronary, cerebrovascular, and peripheral arterial ischemic events as well as ventricular arrhythmias and sudden cardiac death.[5] Curiously, four patients have also been reported to have developed left ventricular (LV) regional ballooning (stress cardiomyopathy [SC]) following cannabis use.[6-9] We hereby present another patient with SC and discuss the underlying pathophysiologic mechanisms for its occurrence following cannabis use.

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There is also evidence that this association is significantly underreported and likely underrecognized.\[9\]

**CASE REPORT**

A 56-year-old Caucasian man with no known past cardiac or neurological history presented to the emergency department with symptoms of confusion, aphasia, and left-sided weakness that started on waking up from sleep. His wife also noted left-sided facial droop and ataxia. He reportedly had increased somnolence, poor appetite, and lethargy for a few days. On presentation, he had a blood pressure of 148/105 mmHg, heart rate of 102 beats per min, rectal temperature of 97.9°F (36.6°C), respiratory rate of 16 breaths per min, and oxygen saturation 98% on room air. On physical examination, he appeared confused, pupils were reactive to light, but there was saccadic eye movement. Motor strength was reduced in the left upper and lower extremities. Computed tomography (CT) and magnetic resonance imaging (MRI) of the head revealed no acute intracranial pathology. In addition, there was no pathology on CT angiography of head-and-neck vessels. Chest X-ray, however, revealed pulmonary congestion [Figure 1a], and ST-segment depression, as well as QTc interval prolongation, was noted on the 12-lead electrocardiogram [Figure 1b]. Serum troponin I was 0.99 ng/ml on admission and rose to a peak of 2.3 ng/m. Urine drug screen was positive for Δ-9-tetrahydrocannabinol (THC) and negative for cocaine, opioids, amphetamines, barbiturates, and benzodiazepines. Blood alcohol and ammonia levels were below reference range. Blood glucose on presentation and thyroid function tests were within normal limits. Transthoracic echocardiogram with intravenous ultrasound-enhancing agent showed a mildly dilated LV cavity with severe hypokinesis of the basal and mid-segments and markedly reduced ejection fraction. The apical segments of the LV, however, showed hyperdynamic motion [Figure 2a, b and Video 1]. Coronary angiography showed no obstructive coronary artery disease [Figure 1c and d]. On further questioning, the patient denied any recent emotional triggers but admitted to heavy marijuana use for several days before this presentation. Cardiac MRI performed 2 days after admission revealed an LV ejection fraction of 36% and hypokinesis of the basal and mid-ventricular segments [Figure 2c, d and Video 2]. No myocardial-enhancing lesions were noted on late gadolinium images. All neurologic and cardiac symptoms resolved after 3 days of treatment. The patient did not return for scheduled postdischarge echocardiography although he was doing well 2 weeks following hospital discharge on a follow-up visit.

**DISCUSSION**

The present case and the few previously reported cases\[5-9\] establish an association between cannabis use and SC [Table 1]. In one of the reported cases,\[6\] repeated exposure to cannabis resulted in recurrence of SC on multiple occasions. We have also shown previously that the association between cannabis exposure and SC is likely significantly underrecognized and underreported.\[9\] The pathophysiology of SC in cannabis users has not been fully understood. However, evidence regarding a direct role of the cannabinoid system in pathogenesis of SC has been accumulating. THC is shown to exert a myocardial suppressant effect through cannabinoid type 1 receptor with downstream signaling that reduces calcium currents and energy production.\[10\] Endocannabinoids released secondary to stress or extrinsic cannabinoid use are known to act on these cannabinoid receptors to cause hypotension, bradycardia, decreased contractility, and myocardial stunning in animal models. In addition, cannabis

![Figure 1](image1.png)  ![Figure 2](image2.png)
use has been shown to cause a hyperadrenergic state through receptor-mediated and receptor-independent mechanisms. The central role of catecholamines in pathogenesis of SC has been proposed based on contemporary observations. It has been thus speculated that SC may represent a form of neurogenic myocardial stunning as the result of centrally triggered release of catecholamines from sympathetic nerve terminals at the myocardium with subsequent cardioinhibitory and coronary vasospastic effects. Based on similarities observed on brain imaging during stress and after exposure to THC, it has also been proposed that amygdala-centered neuronal circuits may underlie the pathogenesis of SC in cannabis users. The combination of cerebral and cardiac events after exposure to cannabis, as observed in our patient, is not surprising as cannabis has been shown to be associated with both stroke and reversible cerebrovascular spasm. Stroke from cannabis use has previously been reported, and the postulated mechanisms include cerebral vasospasm, vasculitis, postural hypotension, and increased carboxyhemoglobin leading to reduced oxygen transportation capacity. In our patient, we also identified a transient metabolic encephalopathy which was likely related to cannabis as no other cause was identified. With this case, we have provided further evidence of an association between cannabis exposures and LV regional ballooning. Although our patient fully recovered from his cerebrovascular and cardiac events, death and recurrent SC have been observed in young individuals after cannabis use. We conclude that cannabis via the endocannabinoid pathway played a key role in the neurological as well as cardiovascular manifestations and this is the first report of concurrent occurrence of both cerebrovascular and cardiac manifestations related to cannabis use.

Research quality and ethics statement

The authors of this manuscript declare that this scientific work complies with reporting quality, formatting, and reproducibility guidelines set forth by the EQUATOR Network. The authors also attest that this clinical investigation was determined to not require institutional review board/ethics committee review, and the corresponding protocol/approval number is not applicable.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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