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RECURRENT CARDIOGENIC SHOCK ASSOCIATED WITH CANNABIS USE: REPORT OF A CASE AND REVIEW OF THE LITERATURE

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☐ **Abstract—Background: The United States has recently undergone increases in the legalization and use of marijuana. There have been previous reports on the association of cannabis use and myocardial dysfunction, however, few on the association with acute stress cardiomyopathy and cardiogenic shock. Case Report: This is a case of a 58-year-old female with a history of inhaled cannabis use, no history of diabetes, and no known history of cardiac disease, that illustrates an association between cannabis use and the recurrent development of stress cardiomyopathy and cardiogenic shock. A review of medical records was performed from two hospitalizations and subsequent outpatient follow-up for similar presentations 6 years apart and review of literature regarding cannabis use and its association with cardiac dysfunction. In separate hospitalizations, the patient presented with clinical findings of cardiogenic shock, severe left ventricular dysfunction with morphologic features of stress cardiomyopathy, and normal coronary angiography. Laboratory results included elevated cardiac biomarkers and urine tetrahydrocannabinol levels > 300 ng/mL. The patient required intensive cardiovascular support, but recovered with normal cardiac function after each event. Why Should an Emergency Physician Be Aware of This?: As use of cannabis becomes more prevalent, it will be important for physicians to recognize the potential association of cannabis use and acute myocardial dysfunction, and how early treatment may contribute to salutary outcomes.** © 2018 Elsevier Inc. All rights reserved.

☐ **Keywords—cardiogenic shock; cardiomyopathy; cannabis; mechanical circulatory support**

INTRODUCTION

Since its recent legalization in multiple states, cannabis use in the United States has increased (1). Whether cannabis, with its predominant psychoactive ingredient tetrahydrocannabinol (THC), can lead to clinically significant cardiac dysfunction, however, is uncertain. A recently published case report identified the occurrence of hemodynamically stable recurrent left ventricular (LV) regional wall motion abnormalities associated with hyperemesis in a chronic cannabis user (2). We present a patient with recurrent reversible life-threatening cardiogenic shock requiring mechanical circulatory support (MCS) who tested positive for high levels of THC in the absence of other identifiable etiologies of myocardial dysfunction.

CASE REPORT

In 2011, a 58-year-old female with a history of labile hypertension and cannabis use, without a history of diabetes or cardiac disease, presented to an outside hospital with

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symptoms of dyspnea and emesis beginning 12 h earlier. Chronic medications included an angiotensin receptor blocker and thiazide diuretic. On presentation, she was afebrile with a blood pressure of 96/52 mm Hg and a sinus tachycardia at 112 beats/min. She had an initial respiratory rate of 24 breaths/min and an oxygen saturation of 100% on room air. Arterial blood gas revealed a pO_2 of 111, pCO_2 of 14, and a pH of 7.56. Within 75 min, oxygen saturation had decreased to 86% on 4 L/m nasal prongs. Chest x-ray study showed pulmonary vascular congestion and interstitial edema. Within 180 min, she appeared "pale, cool, and diaphoretic." Repeat chest x-ray study showed a marked increase in severe pulmonary edema with pleural effusions. On 15 L/m mask, oxygen saturation was 96%. At this point, the emergency physician made the decision to intubate before transfer to the cardiac catheterization laboratory. Electrocardiogram showed non-specific ST changes. Intravenous norepinephrine, vasopressin, dobutamine, and phenylephrine drips were administered to maintain hemodynamic stability.

In the cardiac catheterization laboratory, intra-aortic balloon pump (IABP) was placed. Coronary angiography demonstrated normal coronary arteries. Left ventriculogram in the right anterior oblique view showed several LV systolic dysfunctions with relative preservation of basal function (Video 1). LV end-diastolic pressure (LVEDP) post ventriculogram was markedly elevated at 46 mm Hg (normal ≤12 mm Hg). Thus, given the recognition of progressive cardiogenic shock, a percutaneous transvalvular continuous-flow microaxial mechanical circulatory support device (Impella 2.5; Abiomed, Danvers, MA) was placed.

She was transferred to our center. Echocardiography revealed normal ventricular sizes with an LV ejection fraction (LVEF) of 17% and severe right ventricular systolic dysfunction. Extracorporeal membrane oxygenation (ECMO) was initiated with exchange of the IABP for the ECMO arterial cannula. Microaxial MCS device was continued. Serum lactate was 6.0 mmol/L. Elevated cardiac biomarkers included troponin T of 0.64 ng/mL and N-terminal pro B-type natriuretic peptide (NT-proBNP) of 13,636 pg/mL (reference ranges < 0.03 ng/mL and < 125 pg/mL, respectively). Urine toxicology screen was quantitatively positive for THC at 665 ng/mL (urine levels >15 ng/mL considered positive for smoking one THC cigarette) (3). Urine toxicology screens for amphetamines, barbiturates, cocaine, oxycodone, and phencyclidine on admission were otherwise negative. In-hospital repeat qualitative urine testing 9 days after admission was still positive for THC. In addition to bacterial cultures, acute/convalescent phase viral titers were negative for infection, including Coxsackie B serotypes 1–6 antibodies. Metabolic and hormonal studies excluded thyroid, adrenal, and pheochromocytoma disorders.

Repeat echocardiograms demonstrated gradual improvement in her LVEF to 70%, with removal of all mechanical circulatory support 6 days after admission (Figure 1). At the time of discharge 16 days after admission, she was asymptomatic with ambulation. Before discharge, the patient reported pre-admission daily use of inhaled cannabis. She stated that she had a medical marijuana card and that she did not smoke "until the evenings." Cannabis cessation was recommended.

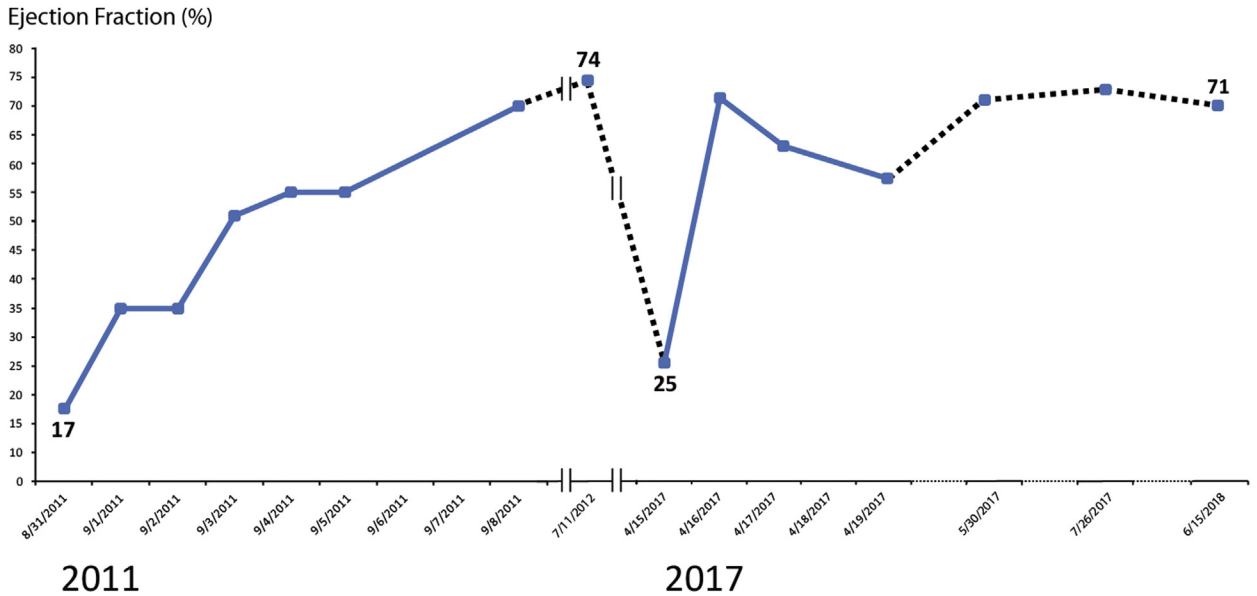

Figure 1. Trend of left ventricular ejection fraction (EF). Left ventricular EF associated with and between two hospital admissions from 2011 to 2017 showing repeated gradual improvement with the use of mechanical circulatory support. Trend in blue shows course of EF improvement during each hospitalization. Dashed lines show time gaps between echocardiograms performed outside of the hospital.

After her initial hospitalization, she had two echocardiograms that showed normal ventricular function. At the time of her second admission in 2017, when she presented to the emergency department with a complaint of dyspnea and recurrent emesis for 12 h, the echocardiogram revealed an LVEF again severely depressed at 25% (Figure 1) with akinesis of the mid to apical 2/3 of the left ventricle (Video 2). Chest x-ray study showed pulmonary congestion. Respiratory rate was 23 breaths/min, with an oxygen saturation of 87%. Bilevel positive airway pressure was initiated. Viral myocarditis panel was again unremarkable.

Aortic pressure was 77/61 mm Hg and heart rate was 77 beats/min in sinus rhythm. Hemodynamics were again indicative of LV dysfunction, with an elevated LVEDP of 24 mm Hg, cardiac output 3.95 L/min, and a decreased cardiac index of 1.98 L/min-m^2 (normal $\geq$ 2.2 L/min-m^2). A percutaneous transvalvular continuous-flow microaxial mechanical circulatory support device (Impella CP; Abiomed), capable of 60% more flow than the microaxial MCS device used in the first admission, was placed. Coronary arteries were again normal by coronary angiography. Laboratory data revealed increased levels of serum lactate (3.8 mmol/L), troponin T (0.44 ng/mL), NT-proBNP (5,966 pg/mL), and positive urine THC levels > 300 ng/mL. Daily echocardiograms showed improvement in LVEF to 71% (Figure 1); microaxial MCS device was removed 2 days after admission and she was discharged 12 days after admission.

DISCUSSION

To our knowledge, this is the first report of a patient with recurrent stress cardiomyopathy and cardiogenic shock associated with use of cannabis. Our patient had emesis with both presentations, suggesting that cannabinoid hyperemesis syndrome may have been an intermediate etiologic factor of her cardiac decompensations (4). Despite life-threatening shock requiring temporary circulatory mechanical support, LV dysfunction was reversible during both hospital admissions.

While stress cardiomyopathy is more commonly associated with emotional and physical stressors, previous reports have suggested a possible association between cannabis use and stress cardiomyopathy, including variable LV contraction morphological patterns and other manifestations of cardiac impairment (2,5–8). Of note, even in the absence of cannabis exposure, severe vomiting has also been reported to be associated with stress cardiomyopathy, possibly associated with increased sympathetic activity (9). The relative contributions of direct cardiac effects of cannabis vs. indirect effects of cannabinoid hyperemesis syndrome are not possible to be determined in this case report.

Potential mechanisms of direct cannabis-associated cardiotoxicity are uncertain. Previous reports have demonstrated the cardiovascular depressive effects of endogenous cannabinoids acting on cannabinoid receptor type 1 (CB1) located on the myocardium and peripheral vasculature, including a negative inotropic effect, as well as modulation of endothelial function resulting in hypotension (10–12). As exogenous THC is known to be a partial CB1 agonist, cardiotoxicity of THC could thus lead to adverse cardiac effects, including stress cardiomyopathy through activation of the endocannabinoid system (8). CB1 has also been implicated in hyperemesis (4).

It is possible that our patient's cardiogenic shock on her first presentation represented a more advanced stage of a continuum and that her second hospitalization was a presentation at an earlier stage. During both admissions, our patient's urinary THC levels were extremely elevated and persisted on her first presentation for at least 9 days after cessation of cannabis use, consistent with a slow rate of drug metabolism. Marked individual diversity in the rate of clearance of THC may occur with reported mean biologic half-lives of THC varying from 1.6 to 57 h (13). Given the scarcity of reports of cannabis-associated clinical cardiotoxicity, it is possible that only patients who accumulate high levels of THC or other clinical factors would be at risk for life-threatening cardiac findings.

In general, initiation of supportive therapy, including mechanical circulatory support for acute non-ischemic cardiogenic shock, can lead to patient recovery (14). Should cannabis use continue to rise, the potential association with reversible profound myocardial dysfunction will be important to recognize.

WHY SHOULD AN EMERGENCY PHYSICIAN BE AWARE OF THIS?

As marijuana use is increasing in the United States with recent legalization, it will become important for emergency physicians to recognize the potential adverse cardiac effects associated with cannabis. Recently, there has been interest in the cannabinoid hyperemesis syndrome and other manifestations of cannabis effects. While reports on cardiac toxicity in association with cannabis use are limited, early recognition and treatment of symptoms can result in improved outcomes.

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SUPPLEMENTARY DATA

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