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Case Report



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Life-threatening constrictive pericarditis accompanied by synthetic cannabinoid use: A case report and literature review

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ABSTRACT

Rationale: Synthetic cannabinoids are increasingly used as recreational drugs and have been associated with adverse cardiovascular effects. However, reports of synthetic cannabinoids accompanied by constrictive pericarditis are limited.

Patient's concern: A 28-year-old male with a history of synthetic cannabinoid (Bonzei) abuse presented with chest discomfort, dyspnea, and lower extremity edema. Investigations revealed reduced left ventricular ejection fraction, elevated inflammatory markers, low electrocardiogram voltages, and atrial fibrillation.

Diagnosis: Chest spiral computerized tomography scan and chest X-ray demonstrated pericardial calcification. Cardiac magnetic resonance imaging and right heart catheterization were done to confirm the possibility of constrictive pericarditis. Based on the patient's addiction history and exclusion of rheumatologic and infectious causes, it was supposed that constrictive pericarditis and cardiomyopathy may be accompanied by synthetic cannabinoid use.

Interventions: The patient received standard medical therapy, including loop diuretics for cardiomyopathy and constrictive pericarditis. Catheter ablation was recommended for his rhythm control, and he was planned for close monitoring of clinical and echocardiographic response and evaluation of the need for surgical pericardiectomy in the future.

Outcomes: After 6 months follow-up, echocardiographic exam revealed no significant improvement in ventricular function. However, due to the high surgical risk, the patient's poor compliance, and the continuation of drug abuse, he was not a good candidate for surgery according to our heart team's decision.

Lessons: Synthetic cannabinoids can trigger constrictive pericarditis, and clinicians should consider them when evaluating patients with

compatible symptoms and exposure history. Further research on the cardiovascular effects of synthetic cannabinoids is needed and public education on potential harms is warranted.

KEYWORDS: Bonzei; Constrictive pericarditis; Synthetic cannabinoids; Cardiomyopathy; Myocarditis

1. Introduction

Psychoactive substances could produce stimulant, depressant, or hallucinogenic effects and have been widely used recreationally and for spiritual purposes throughout human history. In recent years, new psychoactive substances mimicking effects of illegal drugs have emerged[1]. These new substances pose challenges for regulation and healthcare due to the rapid pace at which new chemical variations are introduced once existing compounds become controlled. Synthetic cannabinoids are an example of such drugs that are designed to mimic the effects of cannabis[1]. They were developed initially for scientific cannabinoid research focusing on Δ^9 -tetrahydrocannabinol (THC) as the primary psychoactive

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component of cannabis, cannabinoid receptors, endocannabinoids, and their potential therapeutic applications, but are now synthesized in clandestine laboratories, outside of legitimate research and pharmaceutical contexts, as recreational drugs, and falsely marketed as incense or herbal products[1].

Synthetic cannabinoids have been sold under various names, including “K2”, “spice”, “crazy monkey”, “chill out”, “spice diamond”, “spice gold”, “chill X”, and “Bonzai” since 2004 and are generally smoked or sometimes drunk as tea, primarily by young male adults[2]. The use of synthetic cannabinoids has become a public health concern, as they are often sold as “legal highs” or “designer drugs” and can be easily obtained online or in certain retail establishments[3]. These compounds are often marketed as herbal blends or e-liquids, sold in colorful packets, and designed to evade traditional drug testing techniques[4]. The rapid emergence of new synthetic cannabinoids and their chemical diversity poses challenges in detecting, monitoring, and responding to their use. The United States Drug Enforcement Administration has declared synthetic cannabinoids as Class I controlled substances that are illegal to possess, sell, and use[5].

Synthetic cannabinoids result in a more robust and longer-lasting effect on the body and exhibit exponentially greater potency and efficacy in eliciting cardiotoxicity than THC[6]. Sanchez-Artiles *et al.* identified 25 studies, mostly case reports and series, describing cardiovascular adverse events associated with synthetic cannabinoid consumption[7]. The most frequent adverse events were chest pain, myocardial infarction, acute coronary syndrome, arrhythmias (including atrial fibrillation, ventricular tachycardia, and asystole), and sudden cardiac death[7]. Myocardial ischemia and infarction were precipitated through coronary vasospasm and atherosclerotic complications. Additive toxicity occurs when synthetic cannabinoids are combined with other illicit drugs or alcohol[7]. Myocardial infarctions, cardiomyopathies, cerebrovascular events, and sudden death have been increasingly reported in parallel with escalating synthetic cannabinoid potency[6].

Here, we report a unique case of constrictive pericarditis and cardiomyopathy following habitual chronic synthetic cannabinoid consumption. This report adds to the limited but growing literature on cardiovascular safety concerns with synthetic cannabinoids and highlights the need for further research into their long-term cardiotoxic effects.

2. Case report

The study was conducted in accordance with the principles outlined in the Helsinki Declaration 2008, and approved by the Ethics Committee of Rajae Cardiovascular Heart Center (approval ID: IR.RHC.REC.1402.059). In addition, the patient was given a

participant information statement and signed a written informed consent form. Individual personal information was kept confidential.

A 28-year-old male patient with a history of three years of daily synthetic cannabinoid (Bonzai) abuse presented to the emergency department with complaints of gradually worsening chest discomfort, dyspnea, orthopnea, and leg swelling. Further history-taking revealed no previous systematic disease and nothing specific regarding food or drug allergy. Physical exam showed tachycardia,

Table 1. Baseline laboratory data.

Laboratory test	Reference value	Result
White cell count (cells/μL)	4 500-11 000	6900
Neutrophil (%)	-	57.8
Lymphocyte (%)	-	30.9
Hemoglobin (g/dL)	13.5-17.5	15.6
Platelets ($10^3/\text{mm}^3$)	150-450	131
Sodium (mg/dL)	136-146	137
Potassium (mg/dL)	3.8-5.6	4.4
Calcium (mg/dL)	8.5-10.5	9.1
Creatinine (mg/dL)	0.6-1.4	1.5
BUN (mg/dL)	7-20	32
Pro-BNP (pg/mL)	<125	1 666
CRP (mg/L)	<6	4
ESR (mm/h)	<20	7
FAB (mg/dL)	-	112
TSH (μ IU/mL)	0.35-4.99	2.89
T3 (ng/mL)	0.35-1.93	0.86
T4 (μ g/dL)	4.87-11.72	8.2
LDH (IU/L)	-	513
AST (IU/L)	5-40	22
ALT (IU/L)	5-40	14
Total bilirubin (mg/dL)	0.4-1.5	1.6
Direct bilirubin (mg/dL)	Up to 0.6	0.6
LDL (mg/dL)	Up to 130	53
Triglyceride (mg/dL)	Up to 200	78
Albumin (g/L)	34-53	46
Ferritin (ng/dL)	30-220	79
Serum iron (μ g/dL)	65-175	119
TIBC (mg/dL)	260-468	376
ANA	-	Negative
RF	-	Negative
2ME	-	Negative
Wright	-	Negative
Coombs wright	-	Negative
ACE (IU/L)	8-52	48.2
Anti-CCP (μ mL)	<5	0.5
C3 (g/L)	0.89-1.87	1.7
C4 (g/L)	0.16-0.38	0.22
Anti-Ds-DNA	-	Negative
Quantiferon	-	Negative
HIV Ab	-	Negative
HBS Ag	-	Negative
HCV Ab	-	Negative

BUN: blood urea nitrogen; Pro-BNP: amino-terminal pro-B-type natriuretic peptide; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; FAB: fasting blood glucose; TSH: thyroid stimulating hormone; LDH: lactate dehydrogenase; AST: aspartat aminotransferase; ALT: alanine transaminase; LDL: low density lipoprotein; TIBC: total iron-binding capacity; ANA: antinuclear antibody; RF: rheumatoid factor; 2ME: mercaptoethanol-2; ACE: angiotensin converting enzyme; Anti-CCP: Anti-cyclic citrullinated peptide; HIV: human immune-deficiency virus; HBS Ag: hepatitis B surface antigen; HCV Ab: hepatitis C antibody.

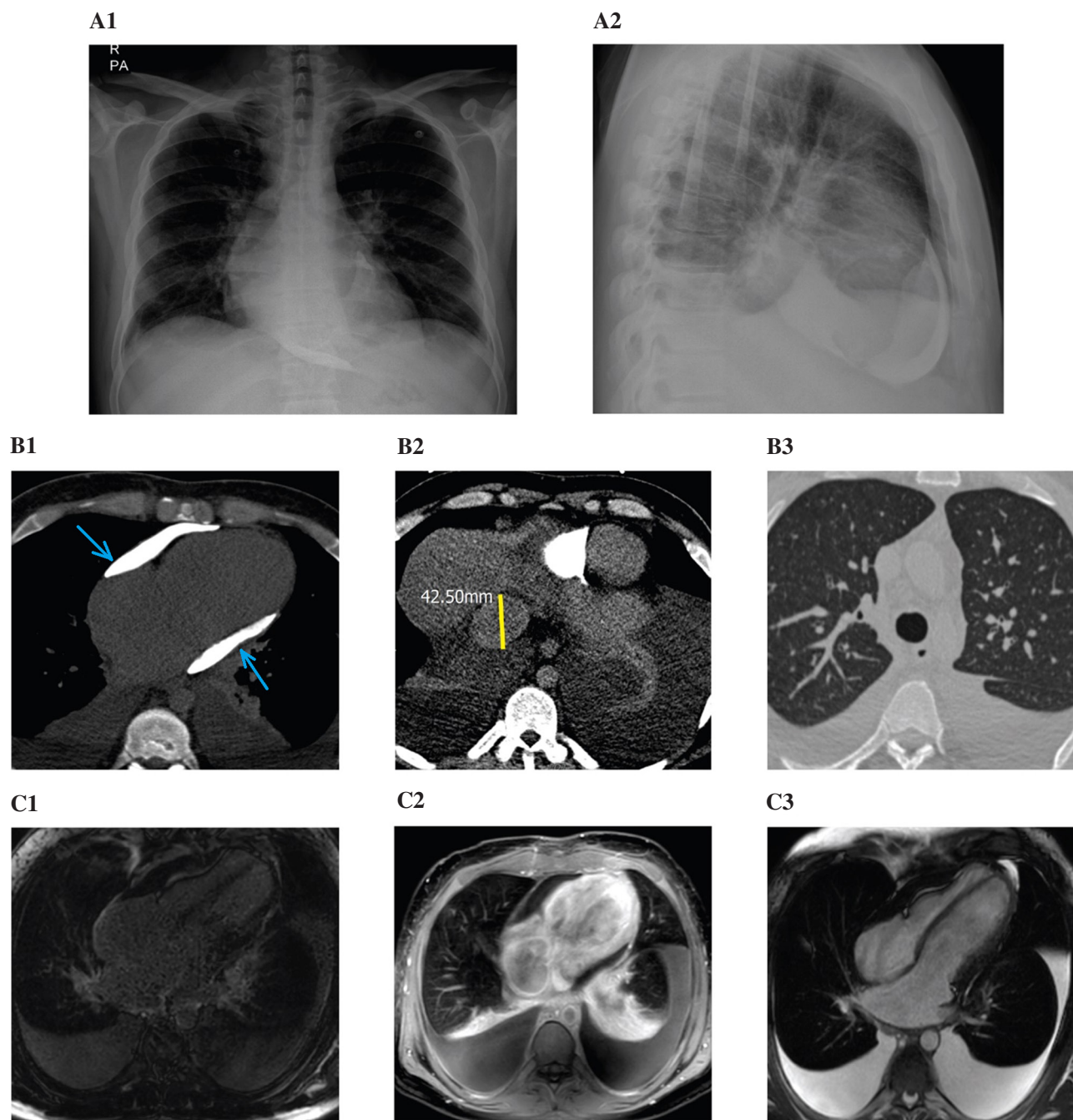


Figure 1. Diagnostic and confirmatory imaging studies of a 28-year-old male patient. Chest X-ray graphs from anteroposterior and lateral views which show linear calcific density overlying pericardium and blunt costophrenic angles better depicted in lateral view, due to bilateral pleural effusion (A1, A2). Axial non-contrast CT scan images, confirm X-ray findings, including smooth diffuse calcific thickening of the pericardium (arrows) with mass effect on cardiac chambers, secondary supportive findings of constrictive pericarditis as dilated inferior vena cava (measured 42.5 mm in anteroposterior view), and bilateral pleural effusion (B1, B2). In lung window diffuse faint centriacinar ground glass opacities, due to synthetic cannabinoid lung injury are also evident (B3). In representative MRI images, the same findings are confirmed (C1-C3). T1 fat saturated with contrast and T2 truefisp images show diffuse low T1, T2 thickening of pericardium without enhancement, bilateral pleural effusion, and mass effect with spade shape cardiac appearance due to underlying constrictive pericarditis.

muffled heart sounds, jugular venous distension, and bilateral lower extremity pitting edema. The patient's 12-lead electrocardiogram (ECG) showed irregular tachyarrhythmia indicating atrial fibrillation and low-voltage QRS complexes in the limb led to the concern of myocardial or pericardial disease. Chest X-ray revealed pericardial calcification (Figure 1A). Additionally, transthoracic echocardiography showed severe systolic dysfunction (left

ventricular ejection fraction of 15%), septal bounce, annulus paradox, annulus reversus, and global hypokinesia with some loss of tissue. Also, it revealed large bilateral pleural effusion, moderate left atrial enlargement, increased filling pressures, and inferior vena cava plethora, all supporting the diagnosis of constrictive pericarditis in addition to heart failure with reduced ejection fraction. Therefore, the patient was admitted to the ward with the impression of constrictive

pericarditis and dilated cardiomyopathy, and initial guideline-directed medical therapy with administration of sacubitril-valsartan, furosemide, digoxin, and eplerenone was started for him.

Detailed laboratory tests and further diagnostic work-up were done to determine the underlying etiology and confirm the diagnosis (Table 1). A spiral computerized tomography scan of the chest revealed thick pericardial calcification surrounding the right atrium, left ventricle, and right ventricle (Figure 1B). Cardiac magnetic resonance imaging showed characteristic findings of constrictive physiology with evidence of myocardial fibrosis without inflammation or edema (Figure 1C). Right heart catheterization was done to confirm the diagnosis and demonstrated equalization of diastolic pressures and ventricular interdependence consistent with constrictive physiology. Coronary angiography revealed patent coronary arteries. The patient did not have a prior history of cardiac or mediastinal surgery, chest radiation, or other rheumatologic or infectious causes to explain his clinical and imaging findings of constrictive pericarditis. Although chronic or repeated idiopathic pericarditis as a cause of constrictive physiology cannot be excluded based on the patient's current history and medical records, we can report a possible cause of synthetic cannabinoid abuse based on his three-year history of regular consumption and exclusion of other possible etiologies.

During the admission, the patient's atrial fibrillation persisted despite the optimization of medical therapy and acceptable rate control. Hence, he was referred for an electrophysiology consult to manage his arrhythmia and evaluate the possibility of tachycardia-induced cardiomyopathy. However, he refused to undergo catheter ablation during treatment, and we planned to monitor his clinical and echocardiographic response to the optimized medical therapy and evaluate the need for surgical pericardiectomy in the future in case of improvement in systolic function. We followed him for 6 months and an echocardiographic exam was performed after heart rhythm control, which revealed no significant improvement in ventricular function. The patient was informed about the need for surgical pericardiectomy. However, due to the high surgical risk and the lack of drug and close-monitoring compliance from the patient, besides the continuation of drug abuse, he was not a good candidate for surgery according to our heart team's decision.

3. Discussion

Recent case reports and preclinical studies have linked cannabis and synthetic cannabinoid use with various cardiovascular complications, including myocarditis, pericarditis, and cardiomyopathy. However, reports of synthetic cannabinoid abuse and constrictive pericarditis are limited. We presented a case of constrictive pericarditis following chronic synthetic cannabinoid abuse, which was simultaneously accompanied by dilated cardiomyopathy without evidence of active myocardial or pericardial inflammation in the cardiac magnetic

resonance imaging study.

Rodriguez-Castro *et al.* reported a case of a 29-year-old previously healthy male patient who presented with acute chest pain on two separate occasions[8]. Both instances occurred after he had smoked adulterated cannabis obtained from Mexico 2-3 days prior. His symptoms were aggravated by lying flat and relieved when sitting up. Lab tests showed elevated inflammatory markers (white blood cells, C-reactive protein, erythrocyte sedimentation rate) and troponin levels. ECG revealed ST elevations consistent with myopericarditis. The echocardiogram was normal except for athletic heart changes. He denied any cannabis use between hospitalizations. During both admissions, his symptoms and ECG findings improved with NSAID treatment. Viral studies were negative. Based on the timeline and resolution of symptoms, adulterated cannabis smoking was implicated as the likely cause of his recurrent myopericarditis. However, angiography was not done to definitively rule out coronary artery disease.

Rahman and Alqaisi similarly reported a case of a 26-year-old male with no significant medical history who presented to the emergency department with acute chest pain[9]. He admitted to daily cigarette smoking and marijuana vaping for years. Lab tests showed elevated cardiac enzymes and inflammatory markers consistent with myopericarditis. ECG revealed sinus rhythm with mild ST elevations in all leads. The echocardiogram showed minimal pericardial effusion and normal ejection fraction. Based on the clinical and diagnostic findings, a diagnosis of marijuana-induced myopericarditis was made. The patient was treated with NSAIDs, colchicine, and pantoprazole. His symptoms resolved with treatment. He was advised to abstain from marijuana use and follow up with a cardiology visit to prevent recurrence[9].

Both cases involved young adult males with recent marijuana use presenting with chest pain. Investigations revealed elevated inflammatory markers and cardiac enzymes with electrocardiographic changes consistent with myopericarditis. Neither had a significant past medical history. The temporal relationship provides circumstantial evidence for a link between cannabis and myopericarditis.

In a study by Rajesh *et al.*, focusing specifically on the role of CB1 receptors in an animal model of diabetic cardiomyopathy, they found that CB1 receptor activation by the endocannabinoid anandamide contributed to oxidative stress, inflammation, cell death, and fibrosis in the diabetic heart[10]. Conversely, CB1 deletion or antagonism with rimonabant attenuated these effects and reduced cardiac dysfunction[10]. Although this study provides evidence from an animal model and describes the pathophysiologic process underlying diabetic cardiomyopathy, we can reasonably conclude that the activation of CB1 by other means, including synthetic cannabinoids, can contribute to promoting cardiac fibrosis and inflammation.

While limited in scope, these cases report instances of myocarditis, pericarditis, and cardiomyopathy associated with cannabis or synthetic cannabinoid abuse. However, establishing a causal link is

restricted by the small number of cases and reliance on self-reported substance use histories. The dilated cardiomyopathy presented in our patient may have additional mechanisms other than synthetic cannabinoid abuse. First of all, drug abusers may deny alcohol consumption due to social or familial issues. Moreover, atrial fibrillation as a baseline cardiac rhythm in our case may be a cause of tachycardia-induced cardiomyopathy. However, the patient's follow-up echocardiogram exam did not show significant improvement in ventricular function even after controlling tachyarrhythmia. Considering all the above-mentioned data, we can report it as a case of constrictive pericarditis accompanying Bonzai abuse, and further researches are required to elucidate its causal relationship. Although a definitive causal association cannot be made based on these limited reports, they highlight the need for caution and awareness of the potential cardiotoxicity risks associated with these substances until more robust evidence is available.

Synthetic cannabinoid abuse may be associated with constriction besides its negative effects on ventricular function. However, further researches are needed to establish its definite causal association. Public health campaigns should educate people about the potential risks of marijuana use, especially for young people and those with underlying health conditions. Patients who use cannabinoids and experience chest pain or other cardiac symptoms should seek medical attention immediately.

Conflict of interest statement

The authors report no conflict of interest.

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Declaration of generative AI and AI-assisted technologies in the writing process

Declaration of generative AI and AI-assisted technologies in the writing process: during the preparation of this work, the authors used Claude 2 to assist with drafting sections of the manuscript and revising the content. After using this service, the authors reviewed and edited the content as needed and took full responsibility for the publication's content.

Data availability statement

The data supporting the findings of this study are available from the corresponding authors upon request.

Authors' contributions

MB: drafting the manuscript. RO: supervision and conceptualization. ZAFJ: investigation and data gathering. AS: investigation, data gathering, and visualization. EK: reviewing and editing the manuscript.

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