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TOXICOLOGY OBSERVATION

K2—Not the Spice of Life; Synthetic Cannabinoids and ST Elevation Myocardial Infarction: A Case Report

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Abstract
Introduction The adverse effects of synthetic cannabinoids are not well-described nor have they been thoroughly studied.
Case Report A 16-year-old male with a past medical history of asthma and attention deficit hyperactivity disorder (ADHD) presented to the emergency department (ED) complaining of 24 h of substernal pressure associated with dyspnea, nausea, and vomiting. He reported smoking tobacco cigarettes daily and occasional marijuana use but denied recent use of marijuana. The initial electrocardiogram (EKG) revealed ST-segment elevations in leads II, III, AVF, and V4-V6. The initial troponin level was reported as 1.47 ng/mL, and the initial creatine kinase MB (CKMB) level was 17.5 ng/mL. The patient admitted to smoking "K2" 60–90 min prior to the onset of symptoms. The patient manifested persistent ST elevations with a peak troponin of 8.29 ng/mL. The urine drug immunoassay was positive for benzodiazepines and opiates. Cardiac catheterization revealed normal coronary arteries, no wall motion abnormalities, and normal systolic function.
Discussion Synthetic cannabinoids may have significant potential adverse effects. Chest pain due to myocardial ischemia is rare in adolescents. When evaluating patients with chest pain, it is important to elicit a detailed drug history, specifically inquiring about synthetic cannabinoid use. Urine drug immunoassays may be unreliable and in this case did not detect synthetic cannabinoids.

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Introduction

The use of illicit drugs continues to be on the rise in the USA [1]. Recently, designer drugs have become more prevalent and widely available. Specifically synthetic cannabinoids have become increasingly popular [2]. These substances contain synthetic indole derivatives that are agonists at the cannabinoid 1/cannabinoid 2 (CB1/CB2) receptors [3, 4]. Some are sold in packages marked "not for human consumption" while others are sold as "incense" or "for aromatherapy only," although it is widely known that they are smoked for their THC-like effects [4, 5]. Synthetic cannabinoids have become widely used due to their commercial availability, a perceived more intense "high" compared with cannabis, and the fact that they are not detected on routine urine drug immunoassays [6–8].

There are several synthetic cannabinoids that are commercially available including those designated as JWH-018, JWH-073, JWH-398, JWH-250, HU-210, and CP-47,497, and its homologues; and oleamide [3]. Synthetic cannabinoids are marketed under a variety of names including Spice, K2, Genie, Sence, Moon Rocks, and Black Mamba, among others [4, 9, 10]. Addiction and withdrawal syndromes have been reported with chronic use of synthetic cannabinoids [9, 10].

A variety of adverse clinical effects have been reported in the setting of synthetic cannabinoid use, including tachycardia, agitation, vomiting, tremor, seizures, myocardial infarction, and transient ischemic attacks [6, 7, 11]. Case reports have suggested a potential for tachyphylaxis, leading to an increased risk for abuse [3, 4, 11]. Synthetic cannabinoids have been reported to exhibit mild monoamine oxidase inhibitor effects raising a theoretical risk for the development of

serotonin syndrome [5]. We describe the first case of ST-elevation myocardial infarction associated with synthetic cannabinoid use in the absence of concomitant cannabis use.

Case Presentation

A 16-year-old male (63.5 kg) presented with 24 h of continuous substernal chest pressure. The patient reported pain that was non-radiating and associated with dyspnea, nausea, and vomiting. He had a past medical history of exercise-induced asthma and attention deficit hyperactivity disorder (ADHD). He denied any recent difficulty with asthma. In addition to an albuterol inhaler, his other medications include aripiprazole and methylphenidate, although he was not compliant with these medications for at least 2 weeks. He was a daily tobacco cigarette smoker and had a remote history of marijuana use, but denied recent use because he was on judicial probation and subjected to frequent urine drug testing. He reported the use of a synthetic cannabinoid, K2, 2 h prior to symptom onset. His initial vital signs included a blood pressure of 127/57 mmHg, heart rate of 82 beats per minute, respiratory rate of 22 breaths per minute, oral temperature of 98.6 °F,, and a pulse oximetry of 100 % on room air. His physical exam, including chest and cardiac exam, was unremarkable.

The initial electrocardiogram (EKG) revealed ST-segment elevations in the inferolateral leads (Fig. 1). The patient received sublingual nitroglycerin (0.4 mg× 4 doses), aspirin 162 mg by mouth, morphine 8 mg intravenously, intravenous lorazepam 0.5 mg×2 doses, and intravenous metoclopramide 10 mg with mild improvement of his symptoms. The patient was then started on a nitroglycerin infusion at 5 mcg/min and titrated to pain relief. The initial troponin concentration in the ED was reported as 1.47 ng/mL (normal 0–0.03 ng/mL), and the initial creatine kinase MB (CKMB) concentration was reported as 17.5 ng/mL (normal 0–7 ng/mL).

On hospital day 2, the chest pain persisted and an echocardiogram was performed and revealed no pericardial effusion, normal cardiac function, and a structurally normal heart. On hospital day 3, the patient was started on a heparin infusion. This was discontinued in anticipation of going to the cardiac catheterization laboratory on hospital day 4 and restarted following return from the cardiac catheterization laboratory. The patient was also started on 80 mg verapamil orally administered on hospital day 3 given the suspicion that the etiology of the chest pain may in part be due to vasospasm. The patient was continued on the nitroglycerin infusion for persistent chest pain until hospital day 4. The patient's EKG continued to demonstrate ST-elevations with a troponin concentration that peaked at 8.29 ng/mL and a CKMB that peaked at 33.9 ng/mL. On hospital day 4, the patient underwent cardiac catheterization revealing normal coronary arteries, no wall motion abnormalities, and normal systolic function.

In this case, the patient admitted to using K2 instead of marijuana because of weekly judicial urine drug testing while on probation after being arrested for selling marijuana. The patient indicated that he was aware the urine drug immunoassays would be negative despite synthetic cannabinoid usage. His urine drug immunoassay was positive for opiates and benzodiazepines only, THC and cocaine were negative; however, this test was done after the patient had received morphine and lorazepam in the ED. Confirmatory toxicologic testing was ordered on the patient's serum, but not completed as the specimen was lost in transit to an outside reference laboratory. The urine drug immunoassays from his weekly testing were negative for THC and cocaine for at least 2 months prior to this event.

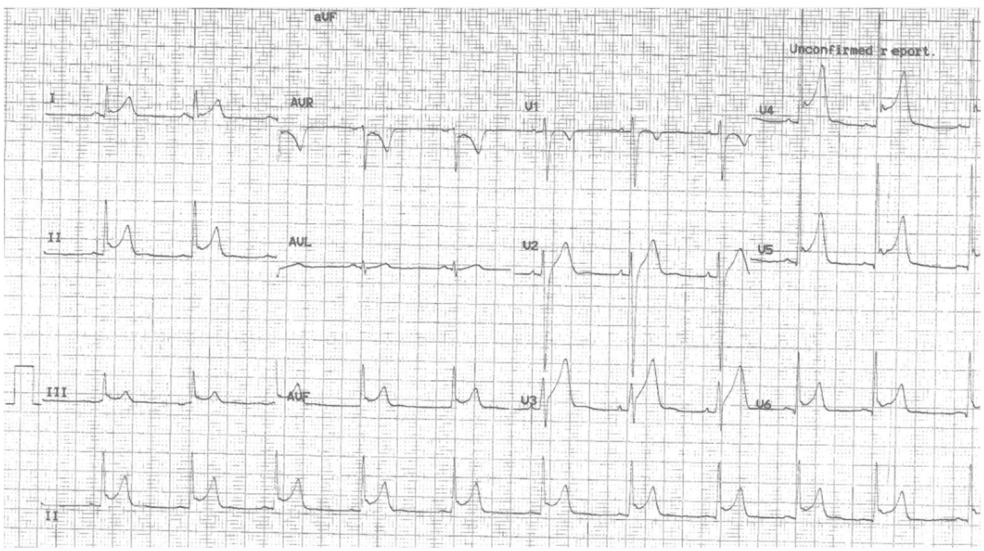

Fig. 1 Patient's initial electrocardiogram

Discussion

Marijuana is currently the most commonly used illicit substance in the USA [1]. Marijuana has been linked to adverse cardiovascular outcomes including tachydysrhythmias, coronary and peripheral artery vasospasm, and myocardial ischemia [12]. Myocardial infarction has been previously reported in the setting of marijuana use [13].

More than 60 different cannabinoids have been identified in marijuana. The most biologically active cannabinoid is Δ^9-tetrahydrocannibol, (THC) [14]. THC has been shown to cause a dose-dependent increase in both heart rate and blood pressure thought to be due to sympathetic stimulation and reduced parasympathetic activity [13]. In a large epidemiological study, marijuana use has been reported to increase the risk of myocardial infarction by 4.8 times in the first hour after use [12]. The proposed mechanisms for cardiovascular events due to marijuana use include an increase in catecholamines, carboxyhemoglobin levels, postural hypotension, increased cardiac workload, and an increase in oxygen demands with a decrease in myocardial oxygen supply [13].

CB1/CB2 are both well-described endogenous cannabinoid receptors. CB1 receptors are concentrated in the brain and spinal cord as well as the peripheral nervous system [3, 4, 9, 12]. Stimulation of CB1 receptors may result in anxiety and euphoria. The CB1 receptor is thought to be responsible for the psychoactive effects of cannabinoids. CB2 receptors mediate immune modulatory effects [3, 4, 9, 12, 15]. As compared to THC, synthetic cannabinoids bind with a greater affinity to the cannabinoid receptors.

A limitation of our case report is the lack of biologic testing of the patient's blood specimen.

Conclusions

Myocardial infarction has been previously reported in the setting of marijuana as well as synthetic cannabinoid use [6, 13]. To our knowledge, this is the first report of ST-elevation myocardial infarction in the setting of synthetic cannabinoid use without concomitant marijuana use. This case suggests an association between the reported use of a synthetic cannabinoid and myocardial infarction. This has been previously reported in teenagers, but a significant limitation of that report, like this one, is the lack of confirmatory testing [6].

While chest pain is not an uncommon presentation in adolescents, chest pain due to myocardial ischemia is rare in this population. When evaluating patients with chest pain, it is important to elicit a comprehensive drug history, including the use of designer drugs such as synthetic cannabinoids. It is important to remember that commercially available urine drug immunoassays are unreliable in this setting and may not detect synthetic cannabinoids.

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