

Synthetic Marijuana Causing Cardiac Arrest and Seizure in A 16-Year-Old Teenager and Review of the Literature

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Abstract

Background: Synthetic cannabinoid abuse has surged significantly in the past few years given the unmonitored online selling and ambiguous marketing. They are often wrongly perceived by teenagers and young adults as “harmless”. They are usually not detected on conventional urine drug toxicology screens. Here we describe a case of brief cardiac arrest within an hour of ingesting synthetic marijuana.

Case presentation: A 16-year-old teenager had an asystolic cardiac arrest lasting for 10 seconds which was documented by cardio-respiratory monitoring in the Emergency Room, followed by a seizure episode within an hour of ingesting synthetic marijuana. He had a full recovery within a few hours.

Conclusion: This adds to the growing evidence of cardiac effects of synthetic cannabinoids which include arrhythmias, cardiac arrest and myocardial infarction.

Keywords: Synthetic marijuana; Cannabinoids; Asystole; Cardiac arrest; Cardiac side effects

Abbreviations: THC: delta-9-tetrahydrocannabinol; CB1: Human cannabinoid receptor 1; CB2: Human cannabinoid receptor 2; ICD: Implantable Cardioverter Defibrillator

Background

Synthetic cannabinoids are man-made chemicals that are applied (often dissolved in a solvent and sprayed) onto plant material or an herbal base that is not marijuana, and are marketed as herbal incense products. They often go by street names such as “K2”, “Spice” and “Black Mamba” [1]. They are a heterogeneous group of compounds, structurally different from delta-9-tetrahydrocannabinol (THC) which is the primary psychoactive ingredient in marijuana, but they are developed to stimulate the human cannabinoid receptor (CB1) and have a much greater binding affinity to CB1. Unlike THC, which is a partial agonist, synthetic cannabinoids are full agonists [2]. The CB1 receptors are present in heart, vasculature, and brain. CB2 receptors on the other hand are expressed primarily in the immune system but recently their presence in myocardium, brain, and smooth muscle cells has been demonstrated [2,3].

Synthetic cannabinoids can be divided into seven main structural groups - Naphthoylindoles (e.g. JWH-018, JWH-073), Naphthylmethylindoles, Naphthoylpyrroles, Naphthylmethylindenes, Phenylacetylindoles, Cyclohexylphenols (e.g. CP 47,497), and Classical cannabinoids (e.g. HU-210). These herbal products were originally available in early 2000's in Europe. By late 2008, synthetic cannabinoids were identified in the United States. The American Association of Poison Control Center's National Poison Data System reported 2869 calls to poison control centers regarding synthetic

marijuana products in 2010 [4]. According to the 2014 National Forensic Laboratory Information System (NFLIS) Special Report, the availability of synthetic cannabinoids has surged significantly since 2010 as indicated by the increase in number of laboratory reports issued in January through June of 2010 (469 reports) compared to January through June 2013 (17241 reports). The NFLIS Special Report also details that the synthetic cannabinoid chemicals identified in laboratory reports from 2010 are vastly different from those chemicals identified in 2013 [5]. Manufacturers of these compounds have modified their chemical structures, sometimes only very slightly, or label them “not fit for human consumption” to evade current laws and regulations to be able to continue marketing these products as “legal highs”. The ingredients are rarely clearly labelled on the packaging, and the brand names vary widely [4]. The popularity of these drugs among youth may be attributed to the fact that the synthetic cannabinoids are widely available (online and at specialty shops) and can rarely be detected in routine urine toxicology screening tests.

Because products marketed as synthetic cannabinoids contain various amounts of different ingredients or combinations that are different from each other, it is difficult to identify which adverse effects are caused by which synthetic cannabinoid chemicals. Synthetic cannabinoids often have a much greater binding affinity to the CB1 cannabinoid receptor than THC found in plant cannabis with *in vitro* and animal *in vivo* studies showing two to one hundred times more potency than THC [2].

Documented adverse effects include hypertension, tachycardia, myocardial infarction, muscle twitches, agitation, psychosis, hallucinations, seizures, stroke, nausea, vomiting, and acute kidney injury [2,8]. A common myth amongst adolescents and adults is that synthetic cannabinoids are safer than non-cannabinoid drugs [4]. A literature search revealed reported cases of myocardial infarction, coronary vasospasm, and cardiac arrest associated with synthetic

cannabinoids in several adults, some with possible pre-existing coronary artery disease, and recently in a 14-year-old boy [9]. A 16-year-old teenager with un-witnessed cardiopulmonary arrest found to be in ventricular fibrillation who had extensive diagnostic work up including a Cardiothoracic angiogram, Cardiac Magnetic Resonance Imaging, Transthoracic echocardiogram, Computed Tomography brain, negative Ajmaline challenge for Brugada, an adenosine challenge for a short PR interval noted on electrocardiogram which produced transient heart block ruling out Wolff-Parkinson White Syndrome, has also been reported. The patient was monitored on telemetry for 13 days and a subcutaneous Implantable Cardioverter Defibrillator (ICD) was placed [10]. Here we report a case of brief asystole lasting for 10 seconds in a teenager, an hour following ingestion of synthetic cannabinoids.

Observation

A 16-year-old previously healthy male was noticed to be walking with an unsteady gait after coming home from meeting his friends at a

local park. He had four episodes of emesis before acute onset of deterioration in his neurological status and rhythmic lip smacking movements concerning for seizure and thus was brought to the Emergency Room by the Emergency Medical Service. The patient was placed on a cardio-respiratory monitor and a laboratory work up was performed which included Serum acetaminophen, aspirin, alcohol levels, complete metabolic panel, and urine toxicology. His potassium was found to be low at 3.1 mmol/L. His initial heart rate was 130 bpm with a QTc of 467 ms. The T waves were normal in morphology. His heart rate gradually decreased and he became bradycardic with a heart rate of 40 bpm. Telemetry showed a notched P wave following which he had a 10 second episode of asystole followed by junctional escape rhythm (Figure 1).

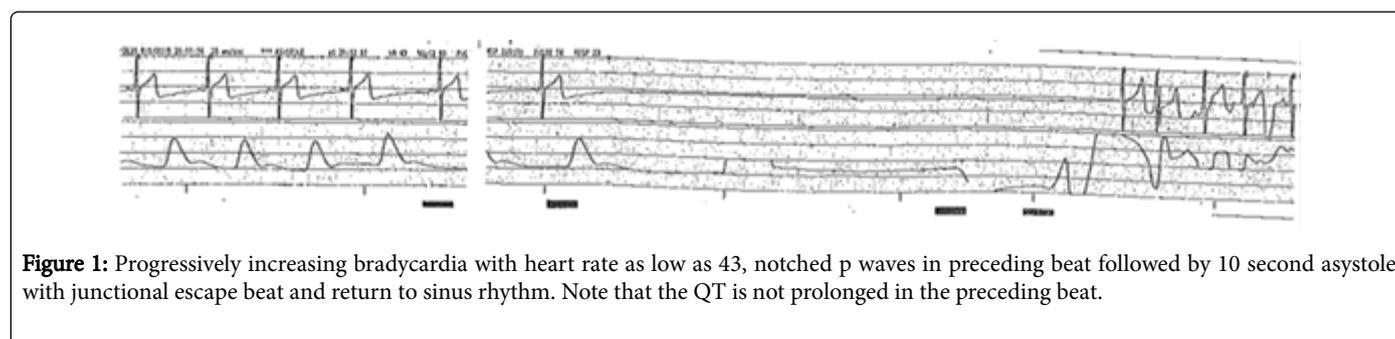


Figure 1: Progressively increasing bradycardia with heart rate as low as 43, notched p waves in preceding beat followed by 10 second asystole with junctional escape beat and return to sinus rhythm. Note that the QT is not prolonged in the preceding beat.

The patient was admitted for further monitoring. His neurological status rapidly improved over the next hour to becoming awake and interactive and admitting to ingesting synthetic marijuana shortly before his symptoms began. His troponin levels were in the normal range. An echocardiogram showed normal cardiac anatomy including normal coronary origins with normal cardiac function. In the context of a negative family history, structurally normal heart on echocardiogram and no further events on telemetry for 48 hours we decided not to insert an Implantable Cardioverter Defibrillator (ICD) or pacemaker. The patient had no further events at 3 months of follow up and a follow up 24 hour Holter monitor showed normal sinus rhythm with no pauses or arrhythmias.

Discussion

Synthetic cannabinoid usage has increased in recent years as a result of relatively easy availability on internet and being sold legally in several countries. They are incorrectly considered benign by the vast majority of teenagers and young adults indulging in substance abuse [4]. The intoxication by cannabis is associated with subjective symptoms of euphoria, perceptual distortion, continuous giggling, sedation, lethargy, impaired perception of time, difficulties in the performance of complex mental processes, impaired judgment and social withdrawal. In addition, physical signs of conjunctival hyperemia, increased appetite, dry mouth and tachycardia can develop. In general, the acute toxicity of cannabinoids is considered to be low. However, there are reports of death by brain infarction, cardiac arrhythmia, acute myocardial infarction, and transitory ischemic attacks. The diagnosis of toxicity is clinical, and standard urine drug screens consist of immunoassays that detect THC metabolites,

primarily THC carboxylase. The lower limits of detection range from 20 to 100 ng/mL, depending upon the specific assay. Confirmatory testing of urine, blood or serum can be sent to reference labs for analysis by gas chromatography and mass spectrophotometry.

There is no specific antidote for cannabinoid toxicity. The treatment is mainly symptomatic with therapeutic options including the use of benzodiazepines, such as lorazepam and alprazolam for anxiety/acute panic disorder, and propranolol to control tachycardia and high blood pressure, antiarrhythmic agents like flecainide, propafenone and digoxin for normalization of the cardiac rhythm and ventilatory support for respiratory depression if needed. Gastrointestinal decontamination with activated charcoal is controversial as most symptoms are delayed up to three hours which limits the efficacy of treatment. Further aspiration is a potential side effect especially if there is respiratory or neurological depression. The standard urine drug screens do not detect synthetic cannabinoids because the synthetic chemical compounds and their metabolites do not cross-react with THC or its metabolites, the agents that these screens are designed to detect. Confirmatory reference laboratory tests via liquid chromatography and mass spectrometry are available but do not return in a timely manner to help with clinical diagnosis and management. If the original product is available, it can often be examined through forensic analytic laboratories with local authorities. However, because the chemical structures and compounds are constantly changing, they can still be difficult to identify, even for reference laboratories.

Not much is known about effects of synthetic marijuana especially on the cardiovascular system. A review of literature showed case reports of myocardial infarction, coronary vasospasm, arrhythmias

and cardiac arrest [6,7]. Several theories have been proposed for the cardiac effects. Gash et al. have shown catecholamine release following ingestion of cannabinoids to cause sympathetic nervous system stimulation which is thought to play a role in sudden cardiac arrest [11]. Some studies have suggested inhibition of sodium and L-type calcium channels by cannabinoids which may explain both seizure activity and asystole in our patient [12]. We report a case of brief asystole lasting for 10 seconds in a teenager an hour following ingestion of synthetic marijuana. It is important to keep synthetic cannabinoids in differential when evaluating arrhythmias including sudden cardiac arrest especially when faced with the question of inserting an ICD in an otherwise healthy young teenager with no significant family history suggestive of a pro-arrhythmogenic genetic milieu, as there are several risks of ICD placement including inappropriate shock delivery, lead fractures, battery replacements, infections, and the need for replacement following device failure or malfunction.

In presence of a clear history or detection of synthetic cannabinoids in a previously healthy young adult or teenager, with no predisposing family history, an ICD placement may not be warranted after a witnessed asystolic event or sudden cardiac arrest in a hospital setting.

Conclusion

In summary, we present the case of cardiac arrest in a previously healthy 16-year-old male within an hour of exposure to synthetic marijuana. As the usage of synthetic cannabinoids increases, it is important to be aware of their potential side effects including cardiac arrest.

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