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CASE REPORT

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Man vs. man-made marijuana: A case of drug-induced posterior reversible encephalopathy syndrome (PRES) due to K2, a ynthetic cannabinoid (SCB)

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ABSTRACT

Synthetic Cannabinoids (SCB) are engineered chemical compounds that share a similar chemical structure with the active ingredient of marijuana, delta-9-tetrahydrocanabinol. Although the FDA has not approved the use of SCB without a prescription from a licensed health-care provider, the cost effectiveness and availability of SCB has made it a popular choice among recreational drug users. Manufacture of SCB as a street drug is not regulated. These SCB are highly potent chemicals that cause various severe toxicities. In this case report, we describe an adult who suffered from PRES after consuming K2, a synthetic cannabinoid.

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1. Introduction

Synthetic cannabinoids (SCB) are man-made psychedelic chemicals that have a similar structure to the active component of plant-based marijuana and act on the same receptor in the brain cells, delta-9-tetrahydrocannabinol receptors [1]. SCB are also known as 'K2,' 'Spice,' 'herbal incense,' 'fake weed', 'mojo', 'cloud 9' and many others [1–3]. These compounds are gaining popularity in the recent years and are becoming a public health hazard, mostly due to their unpredictable toxicity [4]. Consumers use it as a popular alternative to other drugs because of its cheaper price and lack of detection on most standard drug screens. The most common reported toxicities with SCB include agitation, anxiety, tachycardia, hypertension, nausea, vomiting, seizures, tremors, intense hallucinations, suicidal ideation, psychosis, chest pain, and acute kidney injury [2,5]. Here, we report a patient with no prior past medical history who presented to us with new-onset seizure, hypertensive crisis and posterior reversible encephalopathy syndrome following abuse of synthetic cannabinoids.

2. Case presentation

A 54-year-old man presented to our institution with two episodes of witnessed tonic-clonic seizure and altered mental status for several hours. His prior medical history was unremarkable. Upon admission, his vital signs included a blood pressure of 200/129 mmHg, heart rate of 100 beats per minute, respiratory rate of 23 breaths per minute, and oxygen saturation of 100% with 4 L oxygen via nasal cannula. Physical examination was notable for altered mental status and severe agitation without any focal neurologic deficits. The patient was intubated for airway protection. He was treated with intravenous lorazepam, levetiracetam and clevidipine. A complete blood count, comprehensive metabolic profile, serum lactate, blood culture, urinalysis with urine culture, and urine toxicology revealed an elevated white blood cell count of 26,000/mm^3 and an elevated lactic acid at 8.1 mmol/L. Urine toxicology was positive for cannabinoids and benzodiazepines. The remainder of the laboratory studies were normal. The patient was treated with broad-spectrum antibiotics, antiviral agents and fluids. Computed tomography (CT) of head was negative for intracranial hemorrhage. Electroencephalography (EEG) was negative for epileptic activity. Lumbar puncture was remarkable for an increased WBC count of 675/mm^3 and protein of 152 mg/dL. An extensive workup for bacterial, viral, and fungal pathogens associated with central nervous system infection was all negative. While intubated the patient exhibited severe agitation and violent behavior towards health-care providers. He required various interventions including repeated doses of anxiolytics, antipsychotics, sedatives and physical restraints. His severe agitation hindered his ability to get an early brain MRI. Imaging with and without gadolinium obtained 48 h after presentation revealed features concerning for posterior reversible encephalopathy syndrome (PRES) demonstrated in Figure 1. On the fifth hospital day, he was extubated. Following extubation, the patient remained

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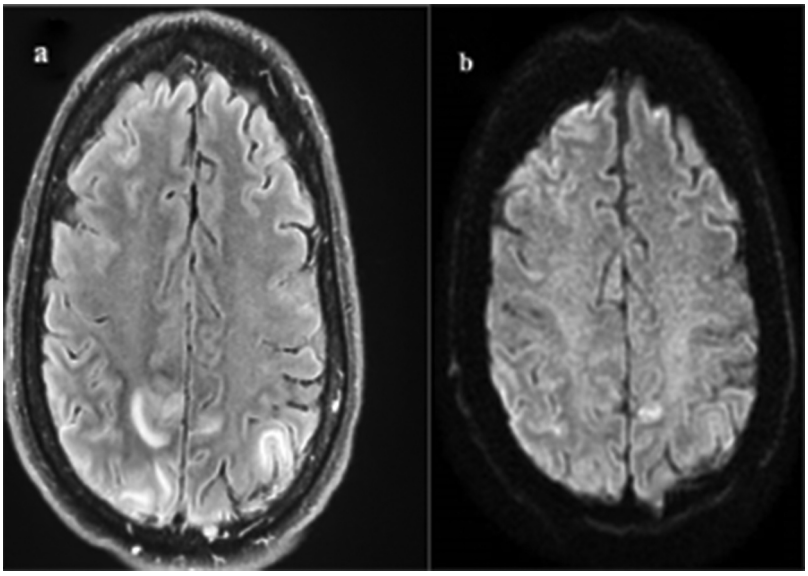

Figure 1. MRI of the brain, Axial view, revealing Posterior reversible encephalopathy syndrome. (a) T2 FLAIR: hyperintensity in the parietal lobes. (b) Diffusion-weighted sequence: diffusion restriction in the parietal lobes.

hemodynamically and neurologically stable and provided a clear social history. He attested to smoking 10–20 g of SCB every day for the past 11 years, and occasional use of plant-grown cannabis. He confirmed the use of a 'new batch of K2' and almost seven episodes of vomiting about an hour prior to the onset of his seizures. Following extubation, the patient expressed a desire to visit with the hospital substance abuse rehabilitation team. However, upon discharge he declined any treatment program for his substance abuse, stating his desire to make changes on his own. Following a week of hospitalization, the patient was discharged to home on oral antihypertensive medications, with a recommendation to follow up closely as an outpatient. Unfortunately, the patient never returned for a follow-up visit.

3. Discussion

Synthetic marijuana is a street drug sold under various names at various convenient stores, tobacco stores and through the internet. SCB are mostly smoked or inhaled while some use it as an additive to herbal teas or food [6]. The major engineered compound in SCB mimics the active constituent, delta-9-tetrahydrocanabinol (THC), of marijuana that binds to the G protein-coupled cannabinoid receptors (CB), cannabinoid receptor 1 (CB1) and cannabinoid receptor 2 (CB2) [2,7,8]. SCB can contain multiple active ingredients and little is known about the metabolism of those compounds [8,9]. Nonetheless, multiple studies have revealed more toxicity associated with SCB compared to marijuana due to the higher potency of the synthetic ingredients [2,8,10,11]. This increased toxicity is mostly explained by the full agonism of synthetic compounds towards CB compared to the partial agonism of THC to CB [10].

The Food and Drug Administration (FDA) has thus far approved three different cannabis-related drug products including dronabinol (oral and liquid formulations), and nabilone [12]. Similarly, there is only one cannabis-derived drug product approved by the FDA, known as cannabidiol [12]. All of the four aforementioned cannabis-like substances are available only by prescription from a licensed health-care provider. Any other form of SCB, such as the one consumed by our patient named K2 (unknown active ingredient), is not approved by FDA for consumption. The unregulated SCB are sold with a disclaimer on the package, 'not for human consumption.' [10,13] The packages of SCB available in the market have various quality and quantity of ingredients. Type and concentration of SCB present between batches of SCB as well as packets of same brand-named SCB can also be variable [6,14].

Although CBs are found predominantly in central nervous system (CB1 receptors) and peripherally in the immune cells (CB2 receptors), both these receptors have also been reported in various other tissues including peripheral nervous system, cardiovascular system, gastrointestinal tract, liver, adipose tissue, bone, and reproductive system [15–17]. Many of the serious adverse effects of SCB toxicity can, therefore, be explained by the presence of CB receptors throughout the body. Table 1 shows various adverse effects of SCB toxicity affecting multiple organs.

SCB intoxication can present as a clinical conundrum. The constellation of clinical effects can range from behavioral abnormalities to more serious consequences including various organ system dysfunction as

Table 1. Most frequently reported adverse effects of SCB in the literature [2,4,7,8,10,11,18–35].

System	Reported side effects of SCB
Neurological	Generalized tonic-clonic seizures, ischemic stroke, acute cerebral ischemia, generalized seizure, status epilepticus, drowsiness, confusion, dizziness, vertigo
Psychiatric	Psychosis, paranoia, self-harm/suicidal ideation, agitation, irritability, hallucination, delusion, catatonia, self-mutilation behaviors, depersonalization, dissociation
Respiratory	Inhalation injury, pneumomediastinum, pneumothorax
Cardiovascular	Myocardial infarction, emboli, tachycardia, arrythmia, chest pain, hypotension, hypertension, bradycardia
Gastrointestinal	Nausea, hyperemesis, appetite changes
Hematology	Coagulopathy, intracranial hemorrhage
Musculoskeletal	Rhabdomyolysis
Renal	Acute kidney injury, acute tubular necrosis, acute interstitial nephritis, acute renal failure
Others including withdrawal symptoms	Death, drug craving, elevated blood pressure, nausea, tremor, diaphoresis, nightmares

described in Table 1. There is no known antidote for SCB intoxication, making supportive care the primary treatment. Standard urine toxicology does not detect SCB, therefore obtaining a detailed history about the recreational use of these substances becomes a paramount to solving the diagnostic dilemma of SCB intoxication. In this case, we believe that the chemicals present in the new packets of K2 caused him to become hypertensive, and rapidly progressed to PRES manifesting as altered mental status and seizures. To our knowledge, this is the first case reporting SCB induced posterior reversible encephalopathy syndrome (PRES). In our patient's case, although common viral etiology as a cause of his clinical manifestations was eliminated, the presence of uncommon viruses was not tested and remains a limitation of our study. Further, patient's urine toxicology upon admission revealed benzodiazepine, yet he refused the use of any other substance except cannabis and SCB. In this setting, the use of any other substance, undisclosed by the patient, cannot be totally excluded. Further, since SCB consumption is a growing public health issue with little understanding of dose-related toxicity future studies on dose-related severity of adverse effects of SCBs are warranted to understand the SCB toxicity better.

4. Conclusion

SCB intoxication can present as a clinical conundrum. One of the serious consequences of SCB intoxication can be PRES encephalopathy. A thorough social history including specific drug histories is paramount to the diagnosis of patients with SCB intoxication. Supportive care remains the standard of care for such patients.

Disclosure statement

The authors declare no conflict of interest.

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References

[1] NIDA. Synthetic Cannabinoids (K2/Spice). National Instituteof Health (NIH). 2018
[2] Mills B, Yepes A, Nugent K. Synthetic cannabinoids. Am J Med Sci. 2015;350(1):59–62.
[3] Gunderson EW, Haughey HM, Ait-Daoud N, et al. "Spice" and "K2" herbal highs: a case series and systematic review of the clinical effects and biopsychosocial implications of synthetic cannabinoid use in humans. Am J Addict. 2012;21(4):320–326.
[4] Bonar EE, Ashrafioun L, Ilgen MA. Synthetic cannabinoid use among patients in residential substance use disorder treatment: prevalence, motives, and correlates. Drug Alcohol Depend. 2014;143:268–271.
[5] Poison Help. The dangers of synthetic marijuana. Texas Poison Center Network. https://www.poison-control.org/the-dangers-of-synthetic-marijuana/
[6] NCEH. About synthetic cannabinoids. Centers for disease control and prevention (CDC). 2017. https://www.cdc.gov/nceh/hsb/chemicals/sc/default.html
[7] Babi MA, Robinson CP, Maciel CB. A spicy status: synthetic cannabinoid (spice) use and new-onset refractory status epilepticus-A case report and review of the literature. SAGE Open Med Case Rep. 2017;5:2050313X17745206.
[8] Alipour A, Patel PB, Shabbir Z, et al. Review of the many faces of synthetic cannabinoid toxicities. Ment Health Clin. 2019;9(2):93–99.
[9] Emery DW, Iceman CR, Hayes SM. Geographic variability of active ingredients in spice as an indicator of mechanisms of distribution and manufacture within alaska. J Young Investig. 2018;34(4):7–16.
[10] Spaderna M, Addy PH, D'Souza DC. Spicing things up: synthetic cannabinoids. Psychopharmacology (Berl). 2013;228(4):525–540.
[11] Andonian DO, Seaman SR, Josephson EB. Profound hypotension and bradycardia in the setting of synthetic cannabinoid intoxication - A case series. Am J Emerg Med. 2017;35(6):940e5- e6.
[12] FDA. FDA and cannabis: research and drug approval process. US Food and Drug Administration (FDA); 2020. https://www.fda.gov/news-events/public-health-focus/fda-and-cannabis-research-and-drug-approval-process
[13] Louh IK, Freeman WD. A 'spicy' encephalopathy: synthetic cannabinoids as cause of encephalopathy and seizure. Crit Care. 2014;18(5):553.
[14] Fattore L, Fratta W. Beyond THC: the new generation of cannabinoid designer drugs. Front Behav Neurosci. 2011;5:60.
[15] Zou S, Kumar U. Cannabinoid receptors and the endocannabinoid system: signaling and function in the central nervous system. Int J Mol Sci. 2018;19(3):833.

[16] Maccarrone M, Bab I, Biro T. et al. Endocannabinoid signaling at the periphery: 50 years after THC Trends. Pharmacol Sci. 2015;36(5):277–296.
[17] Howlett AC, Blume LC, Dalton GD. CB(1) cannabinoid receptors and their associated proteins. Curr Med Chem. 2010;17(14):1382–1393.
[18] Forrester MB. Adolescent synthetic cannabinoid exposures reported to Texas poison centers. Pediatr Emerg Care. 2012;28(10):985–989.
[19] Forrester MB, Kleinschmidt K, Schwarz E, et al. Synthetic cannabinoid and marijuana exposures reported to poison centers. Hum Exp Toxicol. 2012;31(10):1006–1011.
[20] Smith DL, Roberts C. Synthetic marijuana use and development of catatonia in a 17-year-old male. Minn Med. 2014;97(5):38.
[21] Meijer KA, Russo RR, Adhvaryu DV. Smoking synthetic marijuana leads to self-mutilation requiring bilateral amputations. Orthopedics. 2014;37(4):e391–4.
[22] Rojek S, Klys M, Maciow-Glab M, et al. A new challenge in forensic toxicology exemplified by a case of murder under the influence of a synthetic cannabinoid - AM-2201. Leg Med (Tokyo). 2017;27:25–31.
[23] Takematsu M, Hoffman RS, Nelson LS, et al. A case of acute cerebral ischemia following inhalation of a synthetic cannabinoid. Clin Toxicol (Phila). 2014;52(9):973–975.
[24] Hermanns-Clausen M, Muller D, Kithinji J, et al. Acute side effects after consumption of the new synthetic cannabinoids AB-CHMINACA and MDMB-CHMICA. Clin Toxicol (Phila). 2018;56(6):404–411.
[25] McKeever RG, Vearrier D, Jacobs D, et al. K2–not the spice of life; synthetic cannabinoids and ST elevation myocardial infarction: a case report. J Med Toxicol. 2015;11(1):129–131.
[26] Ibrahim S, Al-Saffar F, Wannenburg T. A unique case of cardiac arrest following K2 abuse. Case Rep Cardiol. 2014;2014:120607.
[27] Lam RPK, Tang MHY, Leung SC, et al. Supraventricular tachycardia and acute confusion following ingestion of e-cigarette fluid containing AB-FUBINACA and ADB-FUBINACA: a case report with quantitative analysis of serum drug concentrations. Clin Toxicol (Phila). 2017;55(7):662–667.
[28] Ukaigwe A, Karmacharya P, Donato A. A gut gone to pot: a case of cannabinoid hyperemesis syndrome due to K2, a synthetic cannabinoid. Case Rep Emerg Med. 2014;2014:167098.
[29] Bhanushali GK, Jain G, Fatima H, et al. AKI associated with synthetic cannabinoids: a case series. Clin J Am Soc Nephrol. 2013;8(4):523–526.
[30] Kazory A, Aiyer R. Synthetic marijuana and acute kidney injury: an unforeseen association. Clin Kidney J. 2013;6(3):330–333.
[31] Schneberk T, Valenzuela RG, Sterling G, et al. Hot wax. JEMS. 2015;40(9):44–47.
[32] Zimmermann US, Winkelmann PR, Pilhatsch M, et al. Withdrawal phenomena and dependence syndrome after the consumption of “spice gold”. Dtsch Arztebl Int. 2009;106(27):464–467.
[33] Panigrahi B, Jones BC, Rowe SP. Brodifacoum-contaminated synthetic marijuana: clinical and radiologic manifestations of a public health outbreak causing life-threatening coagulopathy. Emerg Radiol. 2018;25(6):715–718.
[34] Tait RJ, Caldicott D, Mountain D, et al. A systematic review of adverse events arising from the use of synthetic cannabinoids and their associated treatment. Clin Toxicol (Phila). 2016;54(1):1–13.
[35] Centers for Disease C, Prevention. Acute kidney injury associated with synthetic cannabinoid use–multiple states, 2012. MMWR Morb Mortal Wkly Rep. 2013;62(6):93–98.