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SYNTHETIC CANNABINOID INDUCED ACUTE KIDNEY INJURY IN TWO PREVIOUSLY HEALTHY YOUNG MEN

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ABSTRACT
Synthetic marijuana, a synthetic psychoactive substance that causes similar effects as cannabis, is one of the most used illicit drugs in the world. Various terms have been used for these preparations, including SPICE, K2, and SPICE GOLD. On the streets it is called 'bonsai'. Synthetic cannabinoid preparations are more potent and bind more avidly than cannabis to the cannabis receptors in the brain. They have neurologic, cardiovascular, renal and sympathomimetic effects. We report here two previously healthy young men presenting with acute kidney injury (AKI) after using bonsai. Synthetic cannabinoid use should be considered when an otherwise healthy young male presents with AKI. We suggest that synthetic cannabinoids have the potential to be extremely harmful due to their method of manifacture and high potency. The full danger of these drugs has not yet been determined.

INTRODUCTION

Marijuana, also called cannabis, is a green, brown or gray mix of dried, crumbled leaves from the marijuana plant (cannabis sativa). In recent years, a wide variety of synthetic cannabinoid (SC) products have been made available as smoking mixtures that are sold on the internet and in various specialized shops in some parts of the world. These products are usually sold in foil sachets, typically containing 1-3 grams of dried plant matter to which one or more of the cannabinoids have been added. Synthetic marijuana (synthetic Δ 9-tetrahydrocannabinol (THC), bonsai, Jamaican, Jamaican gold...) is a psychoactive substance that causes similar effects as marijuana. It is one of the most frequently used illicit drugs in the world.

SCs and THC, the psychoactive compound of marijuana have chemically similar structural properties. THC, acts on two G protein coupled receptors in the body, CB1 and CB2, cannabinoid receptors. SC receptors have similar effects with THC, and act mostly in the brain and other organs. SCs are proven to be ten times more harmful than THC and most reports of adverse events related to SCs have been with neurologic, cardiovascular, renal or sympathomimetic effects [1].

Most users are young adults, with the desire to experience cannabis-like effects with a substance that cannot be detected on routine drug tests. We report the cases of two young adults who presented with acute kidney injury (AKI) after using bonsai.

Case 1

A 28-year-old male presented to the Emergency Department of Sisli Etfal Education and Research Hospital, Turkey, with fatigue, edema and oliguria since 2 days. He had no prior medical history. The vital parameters were within the normal range, except a sinus tachycardia of 112 beats/min and the remainder of his physical examination was unremarkable. Laboratory studies revealed AKI with a serum creatinine level of 8,22 mg/dl, blood urea nitrogen of 159 mg/dl and urinalysis showed specific gravity of 1.005, 1+ protein and 4-5 white blood cells (WBC) per

high power field with no red cells or eosinophils. Other initial laboratory findings are summarized in Table 1.

Renal ultrasound demonstrated bilateral echogenic kidneys in the normal anatomic position, configuration and size. Antinuclear antibodies (ANA), anti-neutrophil cytoplasmic antibody (ANCA), complement C3, C4, hepatitis and HIV antibody screens were negative. The patient denied use of any medication. Upon questioning about substance use, the patient talked about smoking hookah with 'bonsai', the last time being about two days ago. Urine output was 2, 6 L/24 h on the first day of hospitalization. The spot urine protein/creatinine ratio was normal. Renal biopsy was not performed, because his renal function improved within the first days of admission. He was discharged home with a serum creatinine level of 2,4mg/dl. A follow up serum creatinine a week later was 1, 3 mg/dl.

Case 2

A 19 year-old man with a 7-days history of edema and paresthesia (especially on his left side), reduced urinary output, weakness, intermittent back and flank pain, presented to our institution. He mentioned that he was discharged from Intensive Care Unit voluntarily and had received daily hemodialysis during his 1st week follow-up. He was found unconscious by his family, lying on his left side, after smoking 'bonsai', prior to his Intensive Care Unit hospitalization. On physical examination his blood pressure was 150/90 mmHg, with a pulse of 98 bpm, he was tachypneic and afebrile. He had bibasilar rales and 3+ edema. He was anuric for a week. On his laboratory examination the most significant findings were; a serum creatinine level of 5,8 mg/dl, blood urea nitrogen of 176 mg/dl, creatinine phosphokinase (CPK) level of 4604 U/L, lactate dehydrogenase (LDH) of 876U/L and aspartate aminotransferase (SGOT) 100U/L . Other initial laboratory findings are summarized in Table 2. Rhabdomyolysis-induced AKI was considered and he received three sessions of hemodialysis. On the third day of his hospitalization, his urine was macroscopically hematuric, on microscopic analysis; there was trace protein, 7-8 WBCs, 2-3 red cells per high power field. The investigation results are summarized in Table 2. His renal ultrasound was unremarkable and serologic markers were normal. The chest x-ray showed bilateral pleural effusion and left lung atelectasis. Analysis of the left side pleural fluid obtained by thoracentesis indicated a transudative type. A chest tube was inserted with no complications for two days. Control chest x-ray was performed that showed right basilar effusion and his chest tube was taken out. Neurology consultation for his left sided paresthesia revealed peripheral nerve injury, and he was taken to a rehabilitation program. He received a total of 8 hemodialysis sessions with subsequent improvement in his renal function. His urine output was 1 L/24 h on the fourth day of hospitalization. A 24-hour urine collection contained 900 mg/24h of protein.

A renal biopsy was not performed because of his early recovery. He had oliguric AKI with a peak creatinine of 7,28 mg/dl. His serum creatinine at discharge was 1,4 mg/dl. A follow-up serum creatinine a month later was 0,7 mg/dl.

DISCUSSION

SCs, often called as "synthetic marijuana" are – in reality – very different from marijuana. They contain powerful chemicals called cannabimimetics and can cause dangerous health effects. The drugs are made specifically to be abused. Like many other illegal drugs, synthetic marijuana is not tested for safety, and users don't really know exactly what chemicals they are putting into their bodies [2].

We present the cases of two young adults who presented to our institution with symptoms of fatigue, edema, reduced urinary output and oliguric-anuric AKI after using SPICE. One of these patients had systemic serious problems and received renal replacement therapy, while the other recovered spontaneously with fluid replacement.

In a variety of case reports, the cardiac and neuropsychiatric adverse effects such as tachycardia, seizures, altered mentation, dependence, withdrawal, myocardial infarction, stroke of synthetic marijuana have been mentioned. Recently case reports have revealed acute renal failure as a potentially lethal side effect of synthetic marijuana [3].

In 2011, three cases of SPICE-associated acute coronary syndrome were reported in the pediatric literature [4]. In late 2012, four residents of the same Alabama community developed AKI after using spice. Three of four patients required kidney biopsies. The finding in all of them was acute tubular necrosis (ATN). All showed improvement in renal function without need for renal replacement therapy [5]. In February 2013, Centers for Disease Control and Prevention (CDC) published a notification in which AKI was identified as an unanticipated complication of the SC abuse. Based on this report, 16 patients from five different states in the USA had been hospitalized due to SC-associated AKI in 2012. In half of the patients a renal biopsy was performed; ATN was the most common histologic finding, while acute interstitial nephritis was the second common pathology, seen in the biopsies. No mortality was reported[7]. In March 2013, a young man with acute renal failure, 3 days after smoking SPICE, whose biopsy showed ATN, was reported. His renal function improved with supportive management and no specific therapy was required[8]. In March 2013 four cases of acute SPICE intoxication were reported. All four of these cases presented with neurologic and cardiac symptoms. The distinctive feature of this case analysis was that blood concentrations of the synthetic cannabinoids were determined in all patients and typical metabolites were also detected in the urine [6]. Again in March 2013, a 36 year old male with regular chronic

cannabis use was reported, who presented with acute renal impairment five times in four years [7]. In January 2014 a case report was published, again acute renal failure after SPICE use, but whom required 3 sessions hemodialysis with subsequent improvement in his renal function. His renal biopsy was reported as acute tubulointerstitial nephritis. He was given 4 weeks course of prednisone, and his renal function returned to normal on follow-up[3].

The patients' presentations were similar, in all of these reports; they were mostly young and healthy men with no history of kidney problems. The most common presentation was nausea, vomiting and flank pain after smoking SPICE 2-3 days before. The peak serum creatinine level varied in each report from 3,3-21 mg/dl, with an average of 7,8 mg/dl.

In our cases, two young and healthy adults without previous medical history, presented with fatigue, edema and oligo-anuria almost 2 days after smoking spice-compatible with the literature. Peak serum creatinine levels were 7.2-8.2mg/dl, urine drug screens were clean, no history of nephrotoxic agent use was mentioned. In the previous presentations, most of the cases recovered and creatinine levels turned to normal on follow up without specific therapy.

The pathogenesis of SC-associated AKI remains to be clarified. In our cases a renal biopsy was not performed but in the similar cases published, the most common histopathologic findings were ATN and acute interstitial nephritis. In some of these cases creatinine phosphokinase levels were mildly elevated. In the second case presented here CPK levels were elevated after 1 week from his unconscious period, and his prolonged immobilization, drug abuse history and brown urine on the tenth day is compatible with rhabdomyolysis. Ischemic ATN secondary to hypovolemia could be a possible explanation but the patients did not present with nausea or vomiting.

Table 1. Laboratory values of case 1

	Day 1	**Day 3**	**Discharge**	**1 week follow-up**
White blood cell count (103/mm3)	10.100	10.500	10.200	8.040
Hemoglobin (g/dl)	13,8	14,7	14,5	14,1
Sodium (mEq/L)	136	136	142	141
Potassium (mEq/L)	5,2	5,1	5	4,5
Calcium (mg/dl)	9,05	9,15	9,35	9,36
BUN (mg/dl)	159	128	84	27
Creatinine (mg/dl)	8,22	4,1	2,4	1,32
CPK (U/L)	168	146	142	136
AST (U/L)	9,7	13	15	15
UA	WBCs, protein 1+	Within normal limits	Within normal limits	Within normal range

Table 2. Laboratory values of case 2

	Day 1	**Day 3**	**Discharge**	**1 week follow-up**
White blood cell count (103/mm3)	18.130	22.170	6.720	4.510
Hemoglobin (g/dl)	8,9	8,2	7,2	9,5
Sodium (mEq/L)	126	128	135	135
Potassium (mEq/L)	4,9	5,3	4,6	4,6
Calcium (mg/dl)	7,63	7,7	10,6	9,7
BUN (mg/dl)	176	210	87	28
Creatinine (mg/dl)	5,8	7,28	1,2	0,7
CPK (U/L)	4.604	958	156	152
Amylase (U/L)	91	69	75	72
AST (U/L)	222	72	33	26
UA	WBCs, 3+ protein, 3+ red cells	WBCs, 3+ protein, 3+ red cells	Within normal range	Within normal range

The patients' common history of synthetic marijuana ingestion suggests a possible pathogenic role of its preparation in these patients' AKI. The time of AKI occurrence is consistent with a common toxic exposure. However, due to the small number of patients, the inability to obtain a sample of the synthetic marijuana involved from the patients' serum and urine samples and the lack of specific biopsy findings, it is difficult to argue for a causative role of the preparations in AKI [5].

Synthetic marijuana preparations involve several additives; the causative agent of the AKI in these cases may have been an additive rather than the cannabinoid itself. Information about the ingredients of SCs that are sold on the streets is not enough to make a definite explanation. As written in the previous reports, these SCs may be contaminated with heavy metals and, toxic injury due to direct effect of SCs (or potentially additional compounds) could be responsible [8].

Based on all these cases, we suggest that SCs have the potential to be extremely harmful due to their method of manufacture and high potency. The full danger of these drugs has not been determined yet.

Abuse trends are on the rise; luckily, laboratory testing is available that provides the opportunity to detect these new substances as part of a urine drug screen [9]. They cannot be detected in the routine drug screen so health care providers should consider SC abuse, in other respects healthy young males, presenting with AKI.

REFERENCES

1. Seely KA, Lapoint J, Moran JH, E AL. (2012). Spice drugs are more than harmless herbal blends, a review of the pharmacology and toxicology of synthetic cannabinoids. *Prog Neuropsychopharmacol Biol Psychiatry*, 39, 234-243.
2. 'Synthetic Marijuana Exposures–2014'. Poison Help, AAPCC, http, //www.aapcc.org/alerts/synthetic-marijuana/
3. Militello J., Heath A, Weiss K, Bray N et al. (2014). Acute Renal Failure. *Consultant*, 360, 54(1), 31,
4. Mir A, Obafemi A, Young A, Kane C. (2011). Myocardial infarction associated with use of the synthetic cannabinoid K2. *Pediatrics*, 128, 1622-1627.
5. Bhanushali GK, Jain G, Fatima H, et al. (2013). AKI associated with synthetic cannabinoids, a case series. *Clin J Am Soc Nephrol*, 8, 1-4.
6. Centers for Disease Control and Prevention. (2013). Acute kidney injury associated with synthetic cannabinoid use—multiple states, 2012. *MMWR*, 62, 93-98
7. Abodunde O, Nakdaa J, Nweke N, Levaka Veera R. (2013). Cannabinoid Hyperemesis Syndrome Presenting With Recurrent Acute Renal Failure. *Journal of Medical Cases*, 4(3), 173-175.
8. Kazory A, Aiyer R. (2013). Syntetic marijuana and acute kidney injury, an unforeseen association. *Clinical Kidney Journal*, 6, 330-333
9. Hermanns-Clausen M, Kneisel S, Hutter M, Szabo B, Auwärter V. (2013). Acute intoxication by synthetic cannabinoids – Four case reports. *Drug Testing and Analysis*, 9-10, 790-794.