Synthetic Cannabinoids Associated Acute Kidney Injury: Case Report

Sentetik Kannabinoidler ile İlişkili Akut Böbrek Hasarı

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ABSTRACT Acute kidney injury is a life-threatining disease that requires prompt hospitalization and its treatment is generally based on etiology. Here, we present a case of acute cidney injury related to a kind of synthetic cannabinoids named bonsai in the Istanbul streets. A previously healthy 28-year-old-man was presented to the emergency department with nausea, vomiting and flank pain for two days. Acute cidney injury was detected, after hospitalization renal biopsy performed and it confirmed acute tubular injury. No dialysis required for treatment. He was discharged after ten days of hospitalization with normal creatinine and good health (only with supportive treatment). Because of significant increase of this kind of drug use in our country in recent years, we decided to present this case.

Key Words: Acute kidney injury; kidney tubular necrosis, acute; cannabis

ÖZET Akut böbrek hasarı genellikle hastane yatışı gerektiren, tedavisi etyolojiye göre değişen, hayatı tehdit eden bir hastalıktır. Bu yazıda, İstanbul sokaklarında bonzai olarak isimlendirilen bir çeşit sentetik kannabinoid kullanımı sonucu oluşmuş bir akut böbrek hasarı olgusu sunulmuştur. Öncesinde bilinen bir sağlık sorunu olmayan ve iki gündür olan bulantı, kusma ve böğür ağrısı yakınmaları ile acil servise başvuran 28 yaşındaki erkek hastada akut böbrek hasarı saptandı. Hastaneye yatırıldıktan sonra yapılan renal biyopside akut tubuler hasar tespit edildi. Tedavisi sırasında diyaliz ihtiyacı olmadı. Yatışından on gün sonra, destek tedavisi ile yakınmasız olarak ve normal kreatinin değerleri ile taburcu edildi. Son yıllarda, ülkemizde bu tür uyuşturucu kullanımında artış olduğu düşünülmesi nedeni ile bu olguyu sunmaya karar verdik.

Anahtar Kelimeler: Akut böbrek hasarı; böbrek tübüler nekrozu, akut; hint keneviri

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Acute kidney injury (AKI) is a common disease in society that associated with high mortality. Prognosis differs on type of kidney injury, age and comorbidities. Kidney gets 25% of cardiac output, so that it is very vulnerable for toxic effects of drugs. Drug induced nephrotoxicity can be dose dependent or idiosynchratic.[1,2]

Cannabinoid (marihuana etc.) is well known psychostimulating drug with euphoric effects. Synthetic Cannabinoids (SCs) (spice, spice gold, k2, jamaica etc.) are recently developed and there is very few data about their effects on human body either short term or long term. These drugs have similar psychological and physiological effects with delta9-tetrahydro-

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cannabinol (THC), the psychoactive principle of cannabis.[3,4] It uses several signal transduction mechanims, including activation of potassium channels, inhibiton of voltage dependent calcium channels, the inhibition of adenyl cyclase and the activation of MAP kinase.[3,5]

They are distributed in the form of dried leaves, resin, or powder and are typically a mixture of SCs and herbal additives.[3] Spice (called bonsai in Istanbul) is typically smoked, using a pipe or by rolling in a cigaret paper, but can also be ingested as an infusion, or inhaled.[3]

SCs are used more in developed countries as stimulant substances especially among young people. However, their use has increased in our country in recent years. Many sudden deaths connected to the bonsai have been reported in the news bulletins, in our country, in recent years. There have not been large trials on SCs. Several cases of AKI in the setting of SC use were previously published.[6,7] Here, we represent a case of acute kidney injury due to a SC termed bonsai in our country.

CASE REPORT

A previously healthy 28-year-old-man was presented to the emergency department with nausea, vomiting and flank pain for two days. He denied use of any medications. He also denied using any herbal medications and alcohol. He didn't have any history of non-steroidal anti-inflammatory drugs (NSAID) use, recent syncope or hypotension. Upon further questioning, he admitted to using a drug called bonsai (spice) which is a kind of SC for one year, and reported an increase in the amount and frequency of use over a week prior to admission. Latest, he had used the drug about 48 hours ago. On physical examination, he was afebrile, with a regular pulse rate of 92 bpm, blood pressure of 140/80 mmHg, with no evidence of orthostasis. He did not appear dehydrated. The rest of his examination was unremarkable. He vomited twice. But he drank enough water orally. He had no signs of dehydration. The baseline biochemical parameters on presentation are presented in Table 1. Urinalysis showed 1+ protein, 2-3 white blood cells per high-power field with no red blood cells or eosinophils. Muddy brown casts were not observed. Proteinuria was 300 mg/24 hours. A urine toxicology screen was negative. Serum complement (C3 and C4), anti-nuclear antibody (ANA), anti-neutrophil cytoplasmic antibodies (ANCAs), anti-glomerular basement membrane (anti-GBM) antibody, hepatitis B and C screens, and anti-HIV antibody were negative. His renal ultrasound was within normal limits. Only, bilateral cortical echogenicity was increased slightly. There was no obvious reason spotted for etiology except bonsai. He didn't have anuria or oliguria. His urine output

TABLE 1: Baseline biochemical laboratory data of the patient

	Values	Reference Values
Glucose (mg/dL)	100	(70-106)
Urea (mg/dL)	92	(17-43)
Creatinine (mg/dL)	5.04	(0.6-1.1)
Sodium mEq/L	137	(134-146)
Potasium mEq/L	3.7	(3.5-5.2)
Clorur mEq/L	106	(97-108)
Uric acid (mg/dL)	4.6	(2.6-6)
Calcium (mg/dL)	8.4	(8.5-10.5)
Phosphorus (mg/dL)	5.3	(2.7-4.5)
ALP (U/L)	51	(30-120)
AST (U/L)	35	(0-31)
ALT (U/L)	30	(0-38)
LDH (U/L)	185	(0-247)
GGT (U/L)	22	(0-38)
CK (U/L)	191	(0-145)
Total bilirubin (mg/dL)	0.57	(0.3-1.2)
Total cholesterol (mg/dL)	198	(130-200)
HDL (mg/dL)	33	(>40)
LDL (mg/dL)	135	(100-130)
Triglyceride (mg/dL)	149	(60-150)
Total protein (g/dL)	6.9	(6.0-8.0)
Albumin (g/dL)	4.4	(3.2-5.5)
pH	7.36	(7.35.7.45)
Bicarbonate (mEq/L)	23	(22-26)
CRP (mg/dL)	0.65	(0-0.8)
WBC (/uL)	8600	(4000-10,000)
Eosinophils (/uL)	200	(0-700)
Hb (g/dL)	13.5	(37-47)
Platelet /UI	199 000	(150 000-400 000)

WBC: White blood cells; Hb: Hemoglobin; Htc: Hematocrit; ALP: Alkaline phosphatase; AST: Aspartat aminotransferase; ALT: Alanine aminotransferase; LDH: Lactate dehydrogenase; GGT: Gamma glutamyl transferase; HDL: High density lipoprotein; LDL: Low density lipoprotein; CRP: C reactive protein.

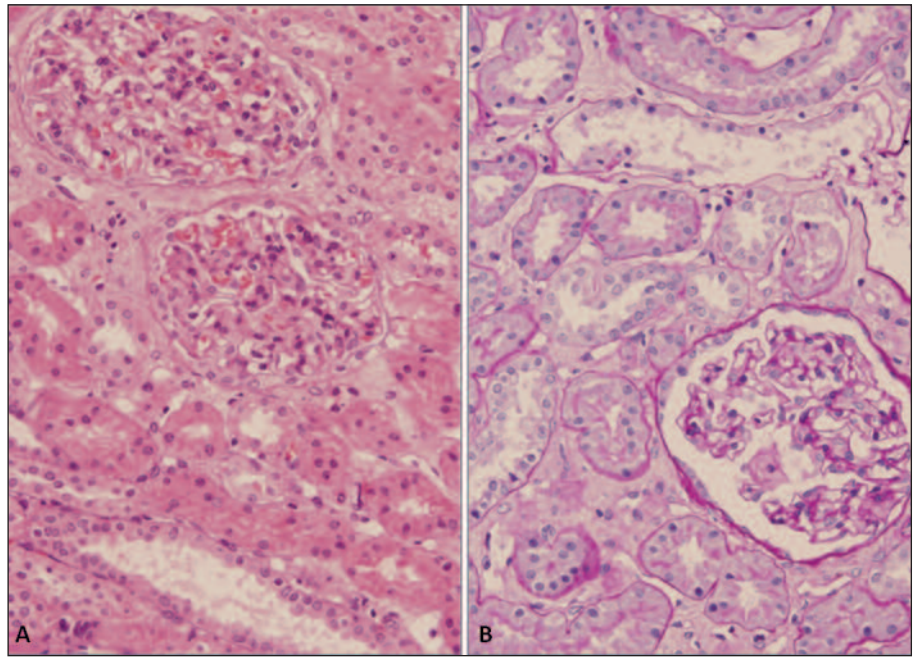

FIGURE 1: Minimal tubular dilatation, flattening of the epithelium, fragments of cells within the tubular lumina, intratubular calcifications and interstitial inflammatory infiltrate with occasional eosinophils (HE 200x).

was about 1500 ml/day on the first day of hospitalization, and had gradually increased in the following days. His symptoms resolved within first day of admission. Although aggressive fluid therapy with isotonic sodium chloride over the next two days, his renal function did not improve. The serum creatinine level had risen up 6.5 mg/dl. Thus, renal biopsy was performed. The biopsy revealed mild acute tubular injury, with minimal tubular dilatation, flattening of the epithelium, fragments of cells within the tubular lumen, intra-tubular calcifications and interstitial inflammatory infiltrate with occasional eosinophils (Figure 1). The glomeruli and the blood vessels were unremarkable, and no immune complex deposits were observed. He did not require renal replacement therapy. The renal functions began to recover after third day of admission. He was discharged home with a serum creatinine of 1.2 mg/dl on the tenth day of hospitalization.

DISCUSSION

Kidney injury related to synthetic cannabis is a new phenomenon. Although cannabis can be used for nausea, these drugs can have side effect as nausea and intractable vomiting can cause hypovolemia, electrolyte disturbances and finally could be a reason for pre-renal AKI.[8] The second theory is that these drugs can cause a myocardial infarction by coronary vasospasm. With the result that the developing heart failure can cause pre-renal AKI. Also, they can cause renal vasoconstriction, and that can leads to ischemic AKI. Besides, they can lead to AKI via rhabdomyolysis. Another theory is direct renal tubular damage and causing nephrotoxicity. As in our case, there are some case reports in all over the world also proving relation to nephrotoxicity.[6,7] Sixteen case of AKI associated use of SCs which was seen in six states of USA, in 2012, have been reported by Centers for Disease Control and Prevention (CDC).[6] Also Bhanushali et al. reported a case series of four patients of AKI associated with spice use.[7] Also, Thornton et al. presented a case of AKI that possibly associated SCs named Mr. Happy.[9] Besides, Bohatyrewicz et al. presented a case of membranous glomerulonephritis that had been seen in a renal transplant recipient may be associated with heavy marijuana

abuse.[10] As a result of the literature screening, there have not seen any case of AKI related SCs except the mentioned cases. Merely, an article in a local newspaper reported 30 cases of AKI among spice users in Casper, Wyoming (mentioned in ref.7). Because SCs is not detected in routine urine drug screens, and generally patients did not admit that they have used the drugs, probably many cases misdiagnosed.

SCs can be determined in the both blood and urine samples by a few methods such as nuclear magnetic resonance, gas chromatography-mass spectrophotometry, liquid chromatography-tandem mass spectrometry and flight mass spectrometry.[11] In addition, saliva and hair samples can be used to determine the substance. Only known substances can be examined by current methods. Therefore it is difficult to determine the new substances.[11]

The major limitation in the interpretation of our case is that we could not determine the toxic substances in the urine. Further, there were no specific biopsy findings. Because of other possible causes of AKI were excluded, and when previously published cases were considered, SCs associated AKI was diagnosed.

Nephrotoxicity mechanism of SCs is still unknown and needs deeper research. There is no enough information about the ingredients in bonsai and other SCs that are sold on the street. Some of the ingredients that we do not know may be added to the drugs. There are still some drugs on streets, even we haven't heard. The number of substances that detectable by current methods is required to increase in order to demonstrate the drug use.

In conclusion, SC addiction is getting a major public health problem in our country and all over the world. SCs should be considered as a possible etiology of AKI especially in young patients with undiagnosed AKI.

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