A New Enemy of the Kidneys: Synthetic Cannabinoids

Böbrekler İçin Yeni Bir Düşman: Sentetik Kannabinoidler

ABSTRACT

Exposure to many different types of substances and drugs may cause acute kidney injury. Beyond the historical well-known ones, we have been experiencing some new, potentially dangerous molecules in recent years and unfortunately among the young population. In this paper, we have presented a case who, following synthetic cannabinoid (Bonsai) use, developed acute kidney injury, received temporary hemodialysis therapy, and fully recovered during follow-up.

KEY WORDS: Synthetic cannabinoids, Acute kidney injury, Hemodialysis

ÖZ

Birçok farklı madde maruziyeti ve ilaçlar akut böbrek hasarına yol açabilir. Bu maddelerden tarihsel olarak iyi bilinenlerin yanında son yıllarda ve de maalesef genç bireylerde yeni, potansiyel olarak tehlikeli moleküllere de rastlamaktayız. Bu yazımızda sentetik kannabinoid kullanımına bağlı akut böbrek hasarı geliştiği için hemodiyaliz tedavisi alan ve izlemde tamamen iyileşen bir olguyu sunduk.

ANAHTAR SÖZCÜKLER: Sentetik kannabinoidler, Akut böbrek hasarı, Hemodiyaliz

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CASE

A 20 year-old-male presented with nausea, vomiting three to four times a day, and abdominal discomfort that had started four days ago. Past medical/family history was not remarkable. He did not describe any nephrotoxic drug or recently commenced alternative therapy in the initial interview. His arterial blood pressure was 150/60 mm/Hg, HR 86/min, and temperature was 36.7^{0}C, without orthostatic symptoms. Pulmonary examination revealed bilateral coarse crackles. The biochemical tests on admission are shown in the table (Table I). Urinalysis revealed density 1005; pH 5.5; protein trace; leu 3; and ery 1. The chest radiography and thorax CT upon admission revealed bilateral pleural infiltration with generalized, patchy, ground glass infiltrations in the upper lung sections in both lungs and specifically in the left lung, and the peripheral lung areas appeared to be substantially maintained (Figure 1A). The creatinine level increased to 7.71 mg/dl during the follow-up; he had metabolic acidosis and his urine output decreased despite intravenous fluid therapy and a temporary non-tunneled hemodialysis catheter was therefore inserted and hemodialysis initiated. Given the co-existence of renal involvement with uncertain etiology and pulmonary radiological findings, pulmorenal syndrome was considered. Bronchoscopy did not reveal endobronchial lesions other than mucoid secretion, and the direct sputum examination did not reveal any findings other than two to three leukocytes in each field. There was no growth in the bronchoalveolar cultures, and the patient was started on empiric antibiotherapy. Meanwhile, the autoimmune markers were negative. Renal ultrasonography revealed kidneys of normal size and parenchymal thickness with bilateral Grade 2 echogenicity and no signs of stones or hydronephrosis. The past medical history of the patient was re-examined in detail, and

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it was ascertained that he had recently used various synthetic cannabinoids (Bonsai) intensively through inhalation. Kidney biopsy revealed increased mesangial matrix in four and slight basal membrane thickening in the other glomeruli. The interstitial area had focal and mild inflammation and focal tubular atrophy. The vascular structures were normal and there was no accumulation in the histochemical staining without signs of acute tubular necrosis (Figure 1B). In total the patient received six sessions of conventional hemodialysis. Following admission, his urination increased as of day 7, and he was taken off hemodialysis on day 9 during the follow up. 24 hour urinary proteinuria was 529.2 mg/day. Pulmonary symptoms and radiological findings regressed but it was not clear whether these lung lesions were attributed to SC use or an infectious agent since cultures were unremarkable. The patient, who had no hypotension, did not use any other nephrotoxic agents was considered to have renal injury resulting from synthetic cannabinoid use. He did not receive any specific treatment other than temporary hemodialysis therapy, antibiotherapy, and support therapy. The creatinine level was 0.93 mg/dl at discharge.

Table I: The biochemical tests at admission.

Urea	60 mg/dl	**AST**	16 IU/L
Creatinine	6.25 mg/dl	**ALT**	13 IU/L
Sodium	135 mmol/L	**LDH**	298 U/L
Potassium	3.8 meq/l	**WBC**	21400
GFR (MDRD)	12 ml/min/1.73m^2	**Hemoglobin**	11.7 gr/dl
Fasting glucose	79 mg/dl	**Hematocrit**	34%
Ph	7.4	**Platelet**	432.000
PCO_2	34.4 mmHg	**ANA**	Negative
HCO_3	20.9 mmol/L	**c/p-ANCA**	Negative
Lac	1.56 mmol/L	**HBsAg**	Negative
Albumin	3.5 gr/dl	**Anti HCV**	Negative
Calcium	9.2 mg/dl	**Anti HIV**	Negative
Phosphorus	5.4 mg/dl	**C3**	122.2 mg/dl
Uric acid	7.2 mg/dl	**C4**	35.6 mg/dl
CRP	28 mg/L	**Creatine kinase**	917 U/L

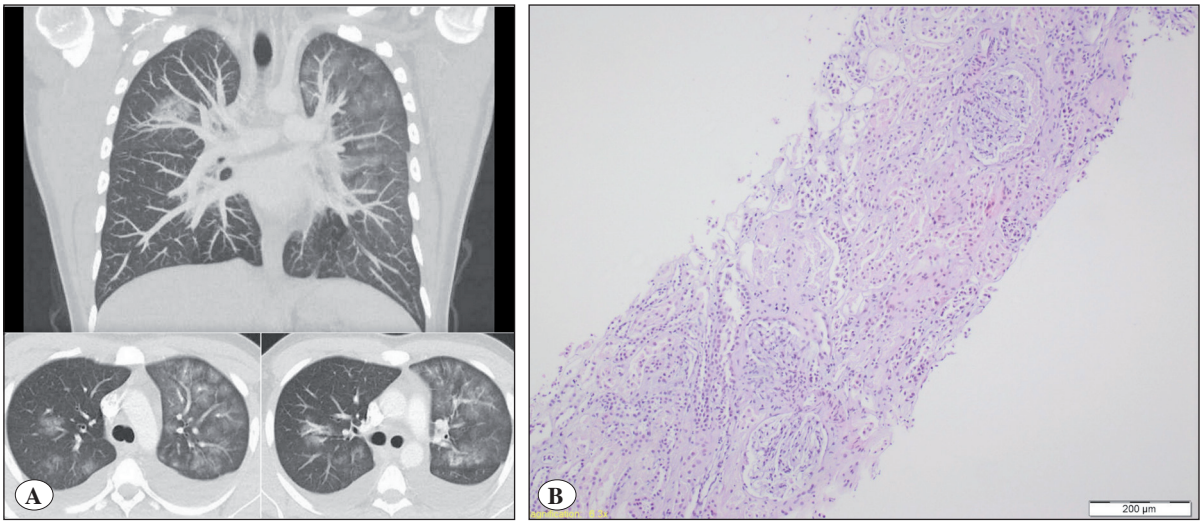

Figure 1:
A) *Thorax CT revealing bilateral pleural infiltration with generalized, patchy, ground glass infiltrations,* ***B)*** *Renal biopsy.*

DISCUSSION

Synthetic cannabinoid related acute kidney injury (SC-RAKI) is described in recent years as a new and poorly understood clinical entity. ATN is known to be the most common finding in kidney biopsies in patients with SC-RAKI. Cannabinoid hyperemesis syndrome is usually the etiology for ATN. The other possible reasons are rhabdomyolysis and tubulointerstitial nephritis (TIN). In the present case, there were no intense vomiting periods, and the kidney biopsy did not reveal any histopathological findings consistent with ATN. The creatinine kinase level of our patient was slightly high and not remarkable for rhabdomyolysis, and the urine findings did not suggest this diagnosis. In addition to these two clinical approaches, unfortunately the pathophysiology of cannabinoid-associated renal injury has not been fully clarified. Due to the pathological findings in renal biopsy and exclusion of other possible etiologies (ATN and rhabdomyolysis), acute renal injury in this patient was attributed to TIN. With respect to cannabinoid-associated kidney injury, the literature also rarely contains cases of acute TIN (1,2). Although acute TIN may be directly caused by the effect of SC, various nephrotoxic chemical substances or heavy metals added to these synthetic compounds that have no standardization may also have an effect on such biopsy results (3). Another interesting point of our case is the resolution of this histopathological picture and the normal kidney function tests without any steroid therapy, and in an unexpectedly relatively short time even though an acute interstitial nephritis pattern was identified in the renal biopsy. In the present case, no specific treatment was administered besides renal replacement therapy. The renal functions improved and the need for hemodialysis was eliminated within an 11-day period. Although the pulmonary involvement upon admission imitated pulmonary-renal syndrome, this diagnosis was excluded through clinical and laboratory findings. The lung involvement with SC use is well described in literature (4). We also think that SC use caused the pulmonary findings in this patient. However, although cultures were negative, infection might have coexisted as CRP regressed with empiric antibiotherapy (ampicillin/sulbactam).

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