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Case Report

Internal Medicine Section

Synthetic Cannabinoid Induced Acute Tubulointerstitial Nephritis and Uveitis Syndrome: A Case Report and Review of Literature

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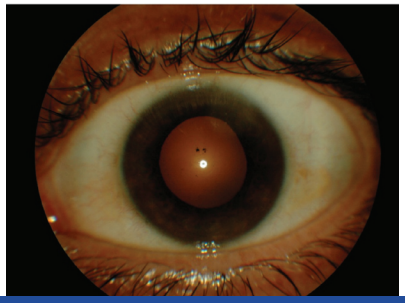
ABSTRACT

Tubulointerstitial Nephritis with Uveitis (TINU) syndrome is a rarely seen syndrome. The interstitial nephritis may be with the concurrent uveitis and can also develop before or after uveitis. The syndrome can resolve after elimination of the culprit destructive factors, such as drugs, toxins and immune reaction. Synthetic cannabinoids have emerged as drugs of abuse with increasing popularity among young adults. Recent literature has documented reports of acute kidney injury in association with the use of synthetic cannabinoids; however, there is no report of TINU syndrome development secondary to using of synthetic cannabinoids. Herein, we report a 42-year-old male with TINU syndrome associated with smoking synthetic cannabinoid.

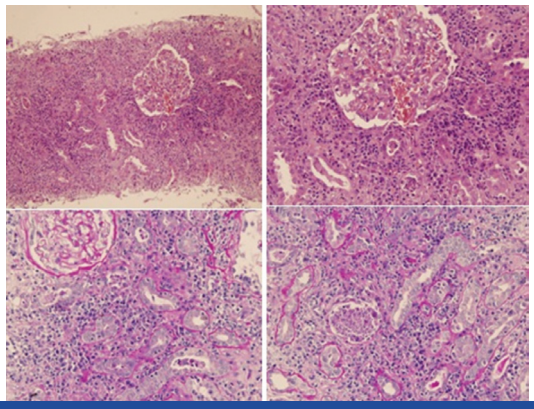
Keywords: Anterior uveitis, Bonsai, Drug abuse, Nephrotoxicity

CASE REPORT

A 42-year-old male was admitted to our hospital because of renal impairment. He had been well until three weeks earlier when he had developed a burning pain and hazy vision in his eyes. The ophthalmologist made a diagnosis of non-granulomatous anterior uveitis and prescribed topical corticosteroid. Two weeks after therapy uveitis improved but thereafter, nausea, vomiting, fatigue, anorexia and flank pain developed. During evaluation of his symptoms, he was detected to have elevated serum creatinine and was referred to nephrology department for further assessment. His past medical history, as well as family history, were unremarkable. He denied intake of analgesics or any indigenous medicine but upon further questioning, the patient admitted to using a synthetic cannabinoid, bonsai, over the prior few weeks. The patient was not critically ill, his appetite was good and there was no recent weight loss. His blood pressure was 140/90 mmHg, pulse 98 beats/min, temperature 37.1°C. All the peripheral pulses were normal and equally palpable. The physical examination was essentially normal; there was no evidence of infection, he had no oedema or palpable lymph nodes and organomegaly. He had no abdominal bruit. The patient also underwent an ophthalmological examination that identified fine keratic precipitations consistent with previous anterior bilateral uveitis. A Schirmer's test performed was normal. Visual acuity was unimpaired and posterior segment examination was normal [Table/Fig-1].



[Table/Fig-1]: Slit-lamp photograph with TINU syndrome showing keratic precipitates.



[Table/Fig-2]: Renal biopsy with hematoxylin and eosin (H&E). Photomicrograph shows an interstitial inflammatory process with associated tubulitis.

His biochemical test results were compatible with acute renal failure {Blood Urea Nitrogen (BUN): 41 mg/dl; creatinine 2.6 mg/dl}. Results of liver function tests and serum calcium, phoshorus, sodium, potassium and other electrolytes were within normal limits. In his blood gas analysis mild metabolic acidosis was detected due to renal impairment (pH:7.29 mmHg HCO_3:19.8 mmol/L); he had a normal haemogram; an elevated erythrocyte sedimentation rate of 64mm/hour, C-reactive protein 24 mg/L (normal: < 5 mg/L). Urine density and pH were within normal ranges with renal glucosuria and absence of any morphologically abnormal cells in the urine sediment. The urine culture was sterile. Complement C3 and C4 levels were within normal limits, Antinuclear (ANA) and Antineutrophil Cytoplasmic (ANCA) antibodies, anti- Glomerular Basement Membrane (GBM) antibody, antibodies to DNA, rheumatoid arthritis factor, SS-A, SS-B, RNP, Sm, Jo-1, Scl70, hepatitis B surface antigen (Hbs Ag) and hepatitis C antibody (HCV Ab) were negative. Chest X-ray was normal; Angiotensin- Converting Enzyme (ACE) level was normal. Ultrasonography of the abdomen did not reveal any abnormality and showed a right kidney of 11.7 cm and left kidney of 12 cm size. As the patient's renal function worsened, with a creatinine of 4.3 mg/dl despite aggressive volume repletion over the next 3 days, a percutaneous renal biopsy was performed on hospital day 4. Eighteen glomeruli were seen by light microscopy and renal biopsy revealed diffuse inflammatory infiltrates with lymphocytic predominance affecting the cortex of the renal tubules and the interstitium with associated tubulitis [Table/Fig-2]. The glomeruli appeared nonproliferative and did not show areas of immune complex deposition by immunofluorescense. These pathological features were consistent with acute tubulointerstitial nephritis. In the presence of biopsy documented acute interstitial nephritis and anterior uveitis,

a diagnosis of TINU syndrome was made. He was started on oral prednisolone 1mg/kg/day and the serum creatinine came down to 1.2 mg/dl in two weeks. The steroid was tapered and stopped after six weeks. He gave up using synthetic cannabinoid, bonsai and is monitored periodically with nephrologic and opthalmologic tests.

DISCUSSION

Tubulointerstitial Nephritis with Uveitis (TINU) syndrome which is rarely seen was first described by Dobrin et al., [1]. They discovered the association between anterior uveitis and non-granulomatous tubulointerstitial nephritis. No identifiable risk factors, such as prior infection or the use of specific drugs {antibiotics, nonsteroidal anti-inflammatory drugs (NSAIDs)}, have been found in at least 50% cases. In a case report, the Chinese herb, "goreisan," has been associated with TINU syndrome [2]. Concurrent infections, such as Chlamydia and Epstein- Barr virus, have been described. It has also been reported that TINU syndrome developed in patients with autoimmune diseases like hypoparathyroidism [3], thyroid disease [4], IgG4-related autoimmune disease [5] and rheumatoid arthritis [6].

Despite the fact that the disease is mostly seen in children and young adults, it can develop in adults and elderly, as well [7]. It is three times more likely to be seen in females than males regardless of particular ethnic affinity [8].

Mandeville et al., have set out the diagnostic criteria for definite TINU which requires the presence of histopathologically confirmed AIN and typical uveitis [9]. The clinical manifestations are stereotyped with alterations in the general condition of the patient and weakness. Our patient had typical symptoms (nausea, vomiting, fatigue, anorexia) according to the diagnostic criteria. Uveitis may occur two months before, concurrently and up to 14 months after the onset of interstitial nephritis. The uveitis is typically anterior, bilateral and nongranulomatous. It often relapses but long term ocular sequelae are rare. The most common ocular complaints were eye pain, redness, decreased vision and photophobia [10]. Our patient was made a diagnosis of non-granulomatous anterior uveitis by ophthalmologist before he was referred to us.

Renal biopsy is a crucial step to establish the diagnosis of TINU syndrome. On light microscopy, The typical findings are tubulo-interstitial oedema and infiltration of inflammatory cells which mainly consist of lymphocytes, histiocytes and plasma cells on light microscopy. In addition, neutrophils, eosinophils and noncaseating granulomas are frequently detected. Vascular structures and glomerular are generally preserved. On immunofluorescence microscopy, the findings are non-specific [11]. In our case renal biopsy was performed and the pathological features were consistent with acute tubulointerstitial nephritis. The risk factors for developing TINU syndrome are infection and drug use such as antibiotics and nonsteroidal anti-inflammatory drugs [12]. Our patient did not use any drugs. Also, TINU secondary to infectious disease was not possible since there were no extrarenal symptoms suggestive of an ongoing infectious process. Moreover, the serological markers for common causative agents of TINU was negative. However, he had been using a synthetic cannabinoid, bonsai, over the prior few weeks and the symptoms began after using bonsai.

SCs, contain powerful chemicals called cannabimimetics and can cause dangerous health effects. Various terms have been used for these preparations, including SPICE, K2 and SPICE GOLD. On the streets it is called "bonsai". Over the past few years, they have been increasingly used for recreational purposes, especially by young adults. A variety of adverse physical and neuropsychiatric effects associated with SC abuse have previously been reported [12,13] but the emerging reports are suggestive of potential nephrotoxicity of these products. Bhanushali et al., reported four cases of AKI associated with SC abuse in Alabama, in 2012 for the first time in the medical literature [14]. Finally, Tait et al., reported a systematic review of adverse events arising from the use of SCs [15]. From 256 reports, they found that the major complications were cardiovascular events, AKI, and generalized tonic-clonic seizures. ATN was the most common histologic finding, while interstitial nephritis was the second common pathology, seen in the biopsies. The patients' presentations were similar, in all of these reports; they were young and healthy men with no history of kidney problems. The most common presentations were nausea, vomiting and flank pain after smoking SPIKE 2 to 3 days before. In our case, a young and healthy adult who had no history of nephrotoxic agent use, presented with nausea, vomiting, fatigue, anorexia and flank pain after using bonsai compatible with the literature. As he had a biopsy-proven tubulointerstitial nephritis and uveitis, the patient was diagnosed as TINU syndrome.

CONCLUSION

In this case, we made a important clinical observation. We report a case of TINU in a adult patient that developed after smoking bonsai. According to our knowledge, this is the first reported synthetic cannabinoid (bonsai) induced TINU syndrome in the literature.

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