

Acute Interstitial Nephritis Induced by *Citrullus Colocynthis*

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Acute interstitial nephritis (AIN) is known as a common cause of acute kidney injury, found in 15% to 27% of kidney biopsies. Drug-induced AIN is currently the most common cause of AIN. The most common medications causing AIN are antibiotics and nonsteroidal anti-inflammatory drugs. We describe a case of *Citrullus colocynthis* (herbal remedy for diabetes mellitus and weight reduction) that induced AIN. A 31-year-old woman with major thalassemia, diabetes mellitus, and hepatitis C infection was admitted because of flank pain and unexpected increase in serum creatinine level. She had been using *Citrullus colocynthis* for 3 months. Kidney biopsy results suggested AIN. She did not respond to steroid therapy and underwent hemodialysis. We suggest the use of *Citrullus colocynthis* as a herbal medicine with extreme caution.

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INTRODUCTION

Traditional customs of plants for medical issues are as old as human civilization.¹ Isolation and biochemical characterization of pharmacologically active compounds from medicinal plants continue today.^{1,2} *Citrullus colocynthis* is a member of the Cucurbitaceae superfamily, with anti-diabetic effects.³ This plant is identified as *Hindal* in Arabian literature and *Abu Jahl* watermelon in Persian language.⁴ Despite medical benefits, some complications such as diarrhea, hematochezia, nephrosis, and liver impairment have been reported.^{5,6} Kidney injury is not explained accurately in different reports.

Acute interstitial nephritis (AIN) is one of the common causes of acute kidney injury (AKI) that is found in up to 3% of all kidney biopsies.^{7,8} Different underlying etiologies are discussed. Drug-induced AIN constitutes approximately 65% of the cases.⁹ We present a case of using *Citrullus colocynthis* for weight reduction that led to kidney failure.

CASE REPORT

A 31-year-old woman with a history of major

thalassemia, diabetes mellitus, and hepatitis C was referred to the emergency department with severe left flank pain. She had used *Citrullus colocynthis* for 3 months and had 6-kg weight loss. Initial evaluation showed urinary tract infection and the patient was discharged with oral antibiotics. One month later, the patient returned with relapse of symptoms. According to mild hydronephrosis on ultrasonography and severe flank pain a double J catheter was placed in. Symptoms did not improve and serum creatinine raised to 7.1 mg/dL. She was treated with antibiotic and hemodialysis, and the creatinine decreased to 2.9 mg/dL.

Urine sediment showed turbid appearance, 2+ protein, blood, more than 200 leukocytes, 10 to 12 erythrocytes, 2 to 3 epithelial cells, and bacteria. Secondary glomerular disease tests are shown in the Table. Urine culture showed greater than 10⁵ *Escherichia coli* colony count. In spite of treatment of infection, there was no change in serum creatinine. Kidney biopsy indicated acute tubulointerstitial nephritis with moderate chronic changes (Figure).

She was treated with prednisolone, 1 mg/kg, for 1 month, and serum creatinine level declined

Laboratory finding of the patient

Parameters	Results
Hemoglobin, g/dL	11.4
Leukocyte count, $\times 10^9/L$	9.3
Platelet count, $\times 10^9/L$	210
Blood urea nitrogen, mg/dL	149
Serum creatinine, mg/dL	4.2
Erythrocyte sediment rate, mm/h	61
Urine pH	6
Complement C3, U/L	0.87
Complement C4, U/L	0.35
Complement CH50, U/L	54.0
Cryoglobuline	Negative
Hepatitis C virus antibody	Reactive
Hepatitis B virus antibody	Negative
Antinuclear antibody	Negative
Double-stranded DNA	7.3
Glomerular basement membrane antibody	4.8
Perinuclear antineutrophil cytoplasmic	2.0
Cytoplasmic antineutrophil cytoplasmic	3.0

to 2.5 mg/dL after 2 weeks of treatment. She was noncompliant to prednisolone. She stopped taking pills and unfortunately came back with rise of serum creatinine and finally hemodialysis began for the patients.

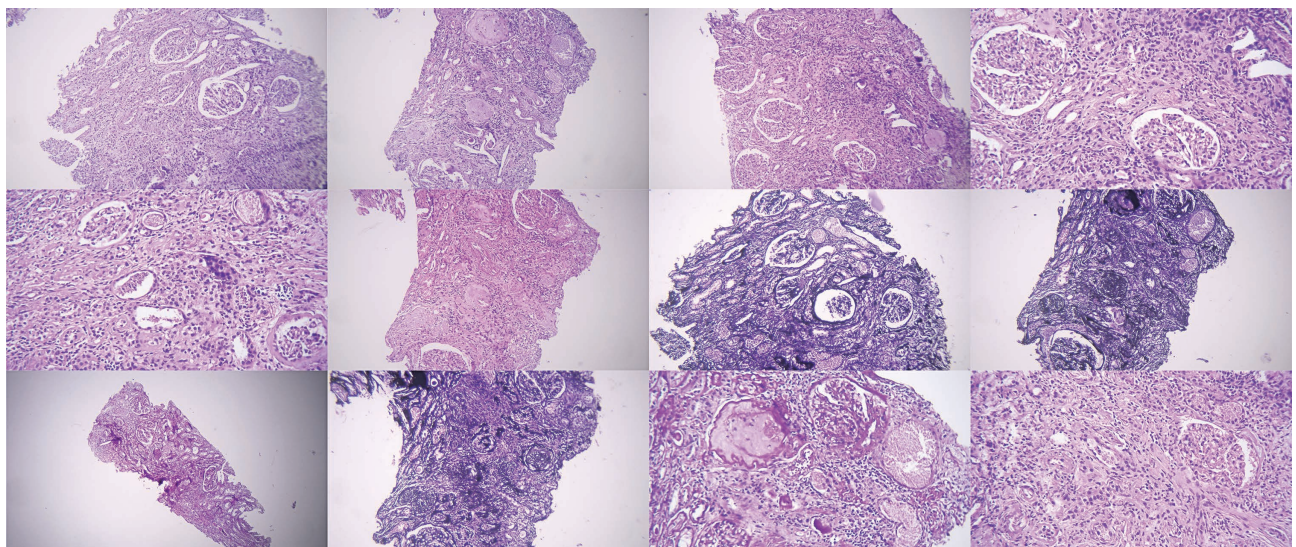
DISCUSSION

We reported a case of AKI caused by *Citrullus colocynthis* that is being used for many medical purposes.⁴ Gastrointestinal, renal, and hepatic

complications have been shown with *Citrullus colocynthis*.⁵ Safe dosage for *Citrullus colocynthis* fruit is suspected 0.6 g to 1.75 g per day. The seed and root should not be administered in the amount of more than 600 and 0.4 g/d, respectively.¹⁰ To our knowledge this was the first report of AIN caused by *Citrullus colocynthis*. Our patient used *Citrullus colocynthis* for a period of 3 months and she had 6-kg weight loss.

Different factors are mentioned in AIN.¹¹ It is often difficult to determine the exact cause of AKI in the patients, especially when they are also receiving several drugs. Drug-induced AINs, such as those due to beta lactams and nonsteroidal anti-inflammatory drugs are suspected the commonest predisposing agents¹²; our patient was receiving both. Hepatitis C virus RNA polymerase chain reaction was undetectable. Major thalassemia can result in focal segmental glomerulosclerosis and nephritic syndrome, but end-stage renal disease is not a common feature for thalassemia. Kidney biopsy revealed tubulointerstitial nephritis and there was no evidence for glomerulonephritis.

Acute kidney injury and tubulointerstitial nephritis caused by nonsteroidal anti-inflammatory drugs and beta lactams are usually reversible by discontinuation of drugs and raise in serum creatinine after acute infectious pyonephritis is considered to resolve by antibiotic administration,



There were 27 glomeruli in the specimen, 8 of which were globally sclerosed. Nonglobally sclerotic glomeruli were normal sized with normal cellularity and no thickening of glomerular basement membrane. There were foci of tubulitis in nonatrophic area that were in favor of acute tubulointerstitial nephritis and there was a large area of tubular atrophy associated with interstitial fibrosis with foci of tubulitis in atrophic tubules that were also in favor of a chronic interstitial nephritis. The amount of tubular atrophy and interstitial fibrosis were about 45% to 50% of tissue surface in favor of severe chronicity of the disease.

but in our patient, serum creatinine did not decline, which is not supported by these medications.

George and coworkers demonstrated that saponins derived from *Citrullus colocynthis* pulp extracts might be the main toxic component of this fruit which has hemorrhagic events in the renal cortex and intestinal mucosa in mice.^{13,14} Shafaei and colleagues reported that toxic side effects of pulp extract at 100 mg/kg/d dramatically exceeded the toxic side effects of seed extract.¹⁵ It is considered that *Citrullus colocynthis* might be safe at a dose of 300 mg/d in 3 divided doses with no serious gastrointestinal and renal complications during 2 months of therapy.

In conclusion, *Citrullus colocynthis* is suspected to induce AIN. This study emerges investigation on the long-term efficacy and toxicity of medical plants to prevent unexpected life-threatening complications.

CONFLICT OF INTEREST

None declared.

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