The Effect of *Tribulus Terrestris* on Acute Kidney Injury: A Case Study

Warning about the Possible Disasters of Self-Prescription of Herbal Medicine

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Herbal medications, such as *Tribulus terrestris*, are widely used, especially by healthy individuals. Despite being easily accessible and perceived as safe, multiple reports have highlighted the potential adverse effects of these medications, although some acknowledge their benefits. In this case report, we present a 43-year-old male patient who has a significant history of self-administered herbal medicine usage. Our aim is to increase awareness about the potential toxicities linked to the use of over-the-counter herbal medicines. Initially, the patient's elevated creatinine level prompted further investigations, which led to the need for dialysis. Following management, he finally survived and recovered; currently, approximately three months later, the patient remains asymptomatic. This case serves as a cautionary example regarding the potential risks of using herbal medications without proper medical guidance.

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Case Report

INTRODUCTION

Herbal medicinal remedies are becoming popular worldwide,[1] with the consumption of over 80%, and 33% in low- and middle-income, and developed countries, respectively.[2] Many use these medications without consulting healthcare professionals,[3] leading to potential risks due to the complex active ingredients and varying side effects of herbal medicines.[4] Some herbs can cause nephrotoxicity, even leading to chronic kidney disease or urothelial carcinoma.[4] Factors contributing to nephrotoxicity include inherent toxicity, processing, contamination, dosage, and interactions with other medications.[4]

Tribulus terrestris (TT) is a widely used plant with diverse medicinal properties;[5-8] including potential renal protective effects;[9-11] however, it could be associated with risks such as hepatorenal syndrome and neurotoxicity.[12-16] In this report, we present a case of acute kidney injury (AKI) attributed to the use of TT; a warning for self-prescribed herbal medicine users and clinicians about the potential toxicities of herbal medications.

CASE REPORT

A 43-year-old truck driver was referred with nausea and weakness. He had been experiencing nausea and vomiting for two months without any signs of hematemesis or other alarming symptoms. The patient denied any clear weight loss; rather, the patient's companion declared a nondocumented weight loss of about 1 or 2 kilograms over these two months, following the onset of nausea and vomiting. He reported constipation but denied having fever, cough, shortness of breath, night-sweats, skin rash, or diarrhea. He had no urinary symptoms. The patient had a history of well-controlled diabetes mellitus, using oral hypoglycemic agents including

Metformin 500mg and acarbose 50mg taken three times a day, for the past two years. He had no previous surgical history, did not smoke, did not use illicit drugs, or did not consume alcohol. The patient mentioned recent use of TT extract as an herbal tea, three times a day, for one to ten days before the onset of symptoms. His allergy history was negative.

Prior to referral to Shohada-e-Tajrish Hospital, the patient was referred to a gastroenterologist for outpatient evaluation of nausea and vomiting; Subsequently, he underwent a gastroesophageal endoscopy with a suspicion of Helicobacter pylori infection and other possible gastrointestinal causes.

Table 1. Laboratory findings of the patient

Measures	Result	Normal Range
Hemoglobin (g/dl)	11.7	12.5-16
Hematocrit (%)	32.6	34-47
Reticulocyte count (%)	0.5	0.5-2.5
Platelet count (x103/µl)	260	150-450
White-cell count (×10^9/L)	7.6	4-11
Neutrophils (%)	62	
Lymphocytes (%)	30	
Monocytes (%)	3	
Eosinophils (%)	2	
Basophils (%)	3	
Serum Creatinine (mg/dl)	15.51	0.7-1.3
Alanine aminotransferase (U/liter)	10	5-38
Aspartate aminotransferase (U/liter)	11	5-42
Alkaline phosphatase (U/liter)	252	80-306
Serum calcium (mg/dl)	9.6	8.5-10.5
Phosphorus (mg/dl)	5.8	2.5-5
Serum magnesium (mg/dl)	2.1	1.5-2.5
Lactate dehydrogenase (U/liter)	266	230-480
Serum Albumin (g/dl)	4.5	3.5-5.5
Serum Uric acid (mg/dl)	8.1	3.6-8
C-reactive protein (mg/L)	21	Up to 10
Erythrocyte sedimentation rate (mm/hr)	51	<15 mm/hr
Serum sodium (mEq/L)	136	135-145
Serum potassium (mEq/L)	4.5	3.5-5.2
Human immunodeficiency virus antibody (HIV Ab)	Non-Reactive	
Hepatitis B surface antigen (HBS Ag)	Negative	
Hepatitis B surface antibody (HBS Ab)	Less than 3.1	
Hepatitis C virus antibody (HCV Ab)	Non-Reactive	
Hepatitis B core antibody (HBC Ab)	0.3	
Serum Iron (µg/dl)	149	70-175
Total iron binding capacity (µg/dl)	170	240-450
Vitamin D_3 (ng/ml)	6.9	>20
Perinuclear antineutrophil cytoplasmic autoantibody (P-ANCA) (U/mL)	Less than 3	<3
cytoplasmic antineutrophil cytoplasmic autoantibody (C-ANCA) (U/mL)	Less than 3	<3
Anti-double-stranded deoxyribonucleic acid antibody (Anti-ds DNA) (IU/mL)	11.6	<15
Antibody to cyclic citrullinated peptides (Anti CCP) (U/mL)	13.3	<20
Glomerular basement membrane antibody (GBM Ab) (EU/mL)	Less than 3	<3
Antinuclear antibody (ANA)	Less than 1/100	<1/100
C3 (mg/dl)	127	75-175
C4 (mg/dl)	31.3	15-45
CH50 (U/mL)	82.9	42-95
Cystatin C (mg/L)	4.89	0.62-1.15
Antistreptolysin O titer (ASO) (IU/mL)	29	<200
Thyroid stimulating hormone (mIU/L)	0.05	0.4-4
Triiodothyronine level, T3 (nmol./L)	1.16	0.9-2.8
Thyroxine level, T4 (µg/dl)	10.29	5-12
T3 resin uptake (%)	25.3	24-37
24 h Urine volume (mL)	500	
24 h Urine creatinine (mg)	513	500-1750
24 h Urine protein (mg)	370	150
Urine Analysis		
SG	1025	
Protein	1+	
WBC	0-1	
RBC	0-1	
Serum protein electrophoresis		
Albumin	61.1%	55.8-66.1%
Alpha 1	2.8%	2.9-4.9%
Alpha 2	12.6%	7.1-11.8%
Beta 1	3.8%	4.7-7.2%
Beta 2	3.8%	3.2-6.5%
Gamma	15.9%	11.1-18.8%
Immunofixation		
Lambda serum	14.5	5.7-26.3
Kappa serum	25.2	3.3-19.4
Immunoglobulin A	63	70-400
Immunoglobulin G	858	700-1600
Immunoglobulin M	35	40-230

Given the normal gastroesophageal endoscopy and absence of any positive findings, only pantoprazole was prescribed to alleviate the patient's symptoms. But the symptoms persisted, and no improvement was observed.

The patient was admitted to Shohada-e-Tajrish Hospital with an elevated creatinine (15.51mg/dl) and blood urea level (184mg/dl); while the patient's baseline creatinine level was 1.1 mg/dl, 3 months prior to the visit. On physical examination, his vital signs were stable, and he appeared well with no other abnormal findings. The initial laboratory examination revealed slightly elevated C-reactive protein (CRP) and Erythrocyte Sedimentation Rate (ESR) levels without leukocytosis. Screening tests for human immunodeficiency virus (HIV) types 1 and 2, as well as immunology assays for rheumatologic diseases, revealed negative results. Thyroid function tests were within normal limits. Further laboratory test results including urine and serum protein electrophoresis are detailed in Table 1.

Further examinations, including chest computed tomography and brain magnetic resonance imaging looking for neurologic defect, did not show any abnormalities. Kidney ultrasound indicated normal kidney size with an increased cortical echogenicity, good cortico-medullary differentiation, and no focal parenchymal lesions or hydronephrosis/hydroureter. A kidney biopsy was performed which revealed acute tubulointerstitial nephritis with acute tubular damage (Figure 1); interstitial fibrosis and tubular atrophy (IFTA) was reported to be 10-15%. No significant glomerulopathy was seen in the immunofluorescence and light microscope studies.

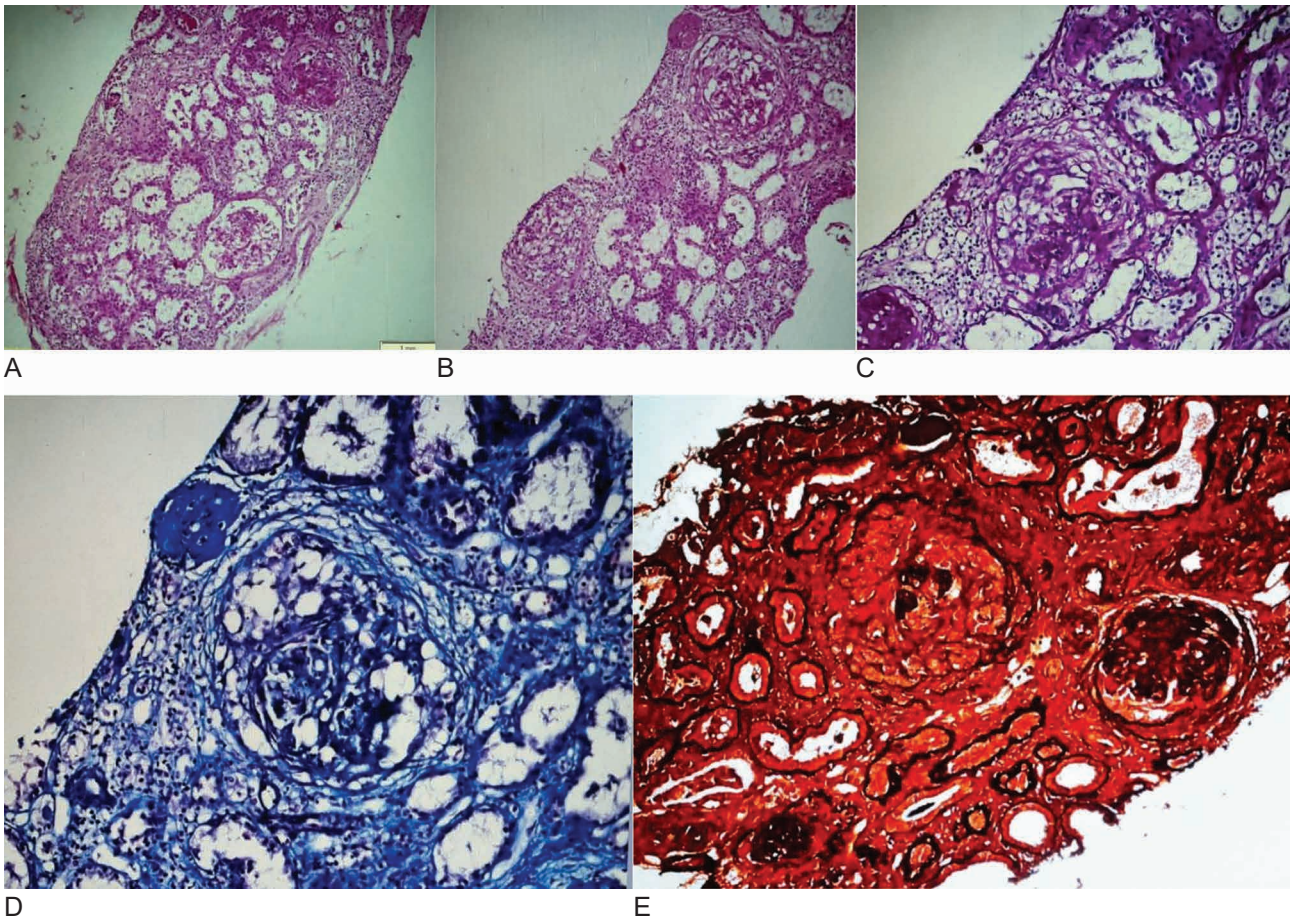

Figure 1. Shows kidney core needle biopsy findings. Serial sections stained by Hematoxylin and Eosin (A, B), periodic acid Schiff (C), Trichrome (D), and Jones' (E) methods show corticomedullary renal tissue with presence of 26 glomeruli that one of them is obsolete. The other glomeruli are preserved and there is no evidence of crescent formation. About 10-15% of the cortical tubules are atrophic and some tubules contain desquamated cells with cellular debris and some tubules contain hyaline casts. Fibrosis is noted around the atrophic tubules but there is edema in most parts with infiltration of lymphocytes admixed with rare neutrophils and eosinophils in 30-40% of the specimen. Mild hyaline arteriosclerosis is present.

The patient underwent eight sessions of hemodialysis and was discharged with improved creatinine level (5.51 mg/dl) after discontinuing the use of TT. After three months, creatinine level decreased to 1.2 mg/dL.

DISCUSSION

This case highlights association between acute kidney injury and consumption of TT, a commonly used herbal product. Herbal products are now widely used worldwide, with many people adopting them into their healthcare practices alongside conventional medicine.[17] Patients often do not disclose their use of herbal medicines to their healthcare providers, making it necessary for healthcare professionals to be vigilant to avoid missing potential diagnoses.

Although herbal remedies are often considered natural and safe, they can have adverse effects, especially on the kidneys; including documented cases of kidney damage in animals following TT consumption.[12,13] On the other hand, the extract of TT was found to have a beneficial effect against certain urinary stone formations.[18]

In this case study, the patient's symptoms were consistent with Acute Tubular Necrosis (ATN) rather than Acute Interstitial Nephritis (AIN). It's worth noting that AIN often occurs shortly after exposure to certain chemical agents;[19] however, our patient's presentation occurred later. AIN typically presents with sterile pyuria, eosinophiluria, and low-grade proteinuria.[19] While the patient's urine analysis showed proteinuria and was negative for eosinophiluria.

Acute Tubular Necrosis (ATN) can occur following exposure to certain toxic substances.[20] A case of ATN following several months of taking TT extracts has been reported in the case report of a young man.[16] Prolonged exposure to toxins can lead to ATN, which typically presents with oliguria, increased sodium fractional excretion, and mild proteinuria;[20] but this toxicity happened following several days of consumption in our case. Management often involves hemodialysis, hydration, and discontinuation of the offending agent.[20]

For a definitive diagnosis, a kidney biopsy was performed, which revealed features of acute tubulointerstitial nephritis with acute tubular damage. No significant glomerulopathy was evident in the biopsy. While casts can be seen in various forms of tubular damage, the possibility of myeloma cast nephropathy should also be considered.[20] In our patient, myeloma kidney was ruled out during the hospital evaluation.

His initial symptoms were nonspecific, and the patient did not exhibit classical urinary symptoms like decrease in urine volume. This highlights the importance of healthcare providers actively inquiring about herbal product usage when evaluating patients with unexplained kidney injury.

Considering the brief period of TT consumption, the patient's prognosis was good. After discontinuing the herb and receiving treatment, such as hemodialysis and hydration, the patient was discharged and there was no longer a need for ongoing dialysis. After three months, creatinine levels returned to baseline, and the symptoms resolved.

In conclusion, it is crucial to remember that herbal products can potentially lead to kidney damage, which may progress to end-stage kidney disease. This emphasizes the importance of obtaining a comprehensive patient history. Therefore, early diagnosis and prompt discontinuation of the causative agent are imperative for achieving a favorable prognosis.

AVAILABILITY OF DATA AND MATERIALS

The datasets are available from the corresponding author on reasonable request.

CONFLICT OF INTERESTS

The authors declare that they have no competing interests

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AUTHORS' CONTRIBUTIONS

MF performed the initial examination of the patient and contributed to the final diagnosis and was a contributor in writing the manuscript. ZP and KKT interpreted patient data, drafted and edited the manuscript. All authors read and approved the final manuscript.

DECLARATION OF PATIENT CONSENT

The authors certify that they have obtained all

appropriate patient informed consent forms. In the form the patient has given his informed consent for his images and other clinical information to be reported in the journal. The patient understands that his name and initials will not be published, and due efforts will be made to conceal his identity, but anonymity cannot be guaranteed.

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