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Case Series

Case series on herbal medication induced acute kidney injury in central India

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ABSTRACT

Around 60 to 70 percent of the people from India reside in rural areas and usually opt for herbal medicine for illness from local traditional medicine practitioners before seeking allopathic advice. Kidneys play a central role in excretion of the metabolites of these substances or the substances themselves. Renal injury happens in the form of acute tubular necrosis, interstitial nephritis, rhabdomyolysis, nephrolithiasis, urothelial cancers and rarely renal cortical necrosis and progressive interstitial fibrosis. Physicians and patients may ignore the potential nephrotoxicity caused by certain herbal medicines, assuming them to be harmless. Adverse event reporting is usually done on a voluntary basis, and toxicity has been reported through case reports and series. It is important for clinicians to factor in the use of herbal medicines when treating patients with unexplained acute kidney injury or progressive chronic kidney disease. We hereby present a case series of renal injury mediated by herbal medications with different mechanism of injury to kidney. This article is first of its type reported from central India.

Keywords: Drug induced AKI, Herbal medicine induced AKI, Acute tubular necrosis, Collapsing FSGS, Acute interstitial nephritis

INTRODUCTION

India is a country of diversity known for various types of heritage and culture. Each state in India is a home to various traditions. The use of herbal medicines is very ancient and almost 50% of drugs of western pharmacopoeia are isolated from plants.[1] Traditional medicine has been practiced for the prevention, treatment, and cure of diseases for thousands of years. The use of alternative remedies derived from plant sources is widely rampant in India especially among the residents of rural communities. Around 60 to 70 percent of the people from India reside in rural areas and usually opt for herbal medicine before seeking allopathic advice.[1] The composition of those drugs vary and they are not tested for adverse effects. Dosage and route of administration of such drugs are not standardized. Herbal medicines may also absorb unknown environmental heavy metals like arsenic, lead, mercury, cadmium which are hazardous.[2] A study conducted in India by Sharma et al showed 29% of AKI presenting in India is due to herbal medicine consumption.[3] Chhattisgarh being developing state in India has forest areas and many tribal communities. And the belief and use of herbal medicine is also very rampant. We report a case series of acute kidney injury caused by herbal medicines in Chhattisgarh, India. This article is first of its type reported from central India.

CASE SERIES

Case 1

A 22-year-old female, second gravida presented at 27th week of gestation with history of decreased urine output for past 5 days and swelling of both lower limbs for past 3 days. Urine output was nil for 24 hours on the day of presentation. Patient was of tribal origin (Gond tribe) and had history of consumption of traditional herb namely

chit-chita [*Achyranthes aspera*] 20 days ago for 1 week in view of generalized weakness and mild stomach ache. On examination patient was normotensive and had mild pedal edema, severe pallor. Investigations summarized in Table 1.

Table 1: Investigation summary of case 1.

Tests	
CBC	Hb- 6, TLC- 5600, Plt- 3.2 lakh
RFT	BU 189, SC- 6.9, potassium- 4.9, sodium- 142
Urine routine	2+ protein, 20-30 RBC, 5-10 pus cells, casts nil
Autoimmune panel	ANA-negative, ANCA-negative, Anti-GBM-negative,
Other investigations	C3 (113 mg/dl) and C4 (29 mg/dl)-normal, LDH 498, PT/aPTT-normal. APLA-negative, viral markers- negative

Ultrasonography revealed normal sized kidneys. Patient was initiated on daily hemodialysis and packed RBC was transfused during dialysis to build hemoglobin to 10. Tunneled internal jugular dialysis catheter was inserted to decrease CRBSI. After 5 consecutive hemodialysis sessions kidney biopsy was done. Kidney biopsy (Figure 1) showed diffuse interstitial inflammation comprising of admixture of lymphocytes, histiocytes, plasma cells and several eosinophils. Tissue for DIF was negative for staining. Patient was diagnosed with acute interstitial nephritis. Patient was treated with pulse methyl prednisolone 500 mg gram for 3 days and later converted to 1 mg/kg oral prednisolone. Patient renal parameters improved after 5 days. Hemodialysis was stopped. Creatinine returned to baseline after 20 days of admission. Both mother and baby were discharged in healthy condition.

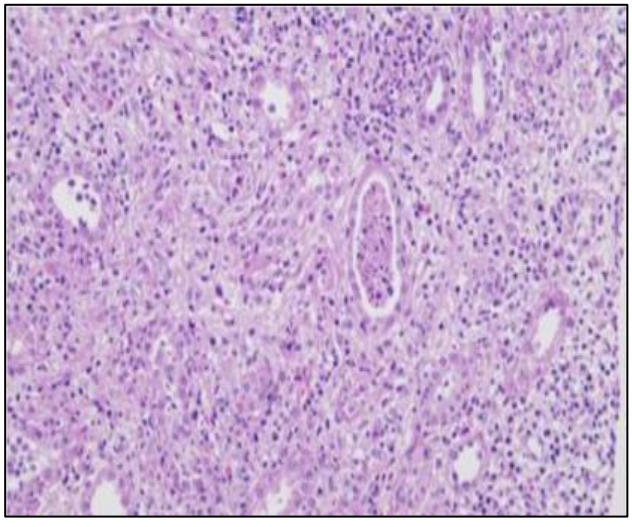

Figure 1: Light microscopy kidney biopsy showing dense lymphocytic infiltrates and tissue edema in interstitial.

Case 2

A 74-year-old male not a known case of any illness presented to emergency with history of breathlessness for past 8 days progressive from NYHA grade 2 to 4 over 8 days. Patient also complained of mild swelling in both legs. Patient had decreased urine output for past 3-4 days and had nil urine output for past 12 hours on the day of presentation. Patient had recently started consuming herbal compounds as immunity boosters namely ashwagandha [contains alkaloids and steroidal lactones], triphala [combination of *Emblica officinalis*, *Terminalia bellerica*, *Terminalia chebula*], muktavati [*Tinospora cordifolia, Withania somnifera*, giloy] two to three times in a day. On examination patient had pulse of 88/min, blood pressure of 210/110 mm hg, respiratory rate of 30 /min, JVP increased. Heart sounds were normal. Bilateral basal fine crepitation were present. Patient was admitted as a case of accelerated hypertension with acute kidney injury in ICU. At admission investigations summarized in Table 2

Table 2: Investigation summary of case 2.

Tests	
CBC	Hb-10.9, TLC- 4900, platelets-2 lakh
RFT	BU-145, SC-9.3, potassium 5.4
Urine routine	3+ protein, 5-7 RBC, 10-15 WBC, No casts
UPCR	6
Auto-immune workup	ANA, ANCA, anti-GBM-negative
Other investigations	Albumin- 2.5, C3 (98 mg /dl)-normal, C4 (30 mg/dL) - normal, LDH-488, viral markers- negative, CT angiography-Normal renal arteries, serum protein electrophoresis-Normal

Ultrasound showed normal sized kidneys with increased cortical echogenicity. Hemodialysis was Initiated after placing right IJV temporary dialysis catheter. Patient developed complete anuria for next 7 days. Renal biopsy was done on day 7 of admission after adequate BP control was achieved. Biopsy showed FSGS involving 2/24 glomeruli with collapse of glomeruli. Severe acute tubular injury was noted. Electron microscopy revealed diffuse effacement of visceral epithelial cell foot process and tubular cytoplasmic vacuoles and phago-lysosomal bodies (Figure 2). Patient remained dialysis dependent for one month after admission. Patient was initiated on prednisolone 1 mg/kg and gradually urine output of the patient improved. Patient was discharged with nadir creatinine of 2.0. 24-hour urine protein was 17 gm/day. Patient received 4 months of high dose steroid following which he attained remission. Gradually steroids were tapered and stopped.

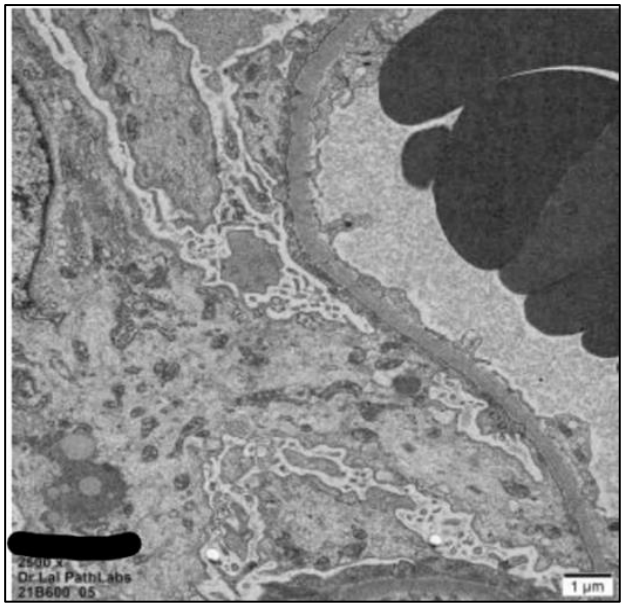

Figure 2: Electron microscopy showing diffuse effacement of foot process with few electrons dense deposits.

Case 3

A 14-year-old male got admitted with swelling of legs since past 1-month, decreased urine output for past 3 weeks. Patient had taken vetasa [salix caprea], 2 weeks ago for 5 days for cold and cough. On physical examination pulse 75/min, bp-102/62, RR 20/min, pallor and edema was present. At admission investigations summarized (Table 3).

Table 3: Investigation summary of case 3.

Tests	
CBC	Hemoglobin- 11.5, TLC- 10000/mm^3, platelet- 3 lakh
RFT	Urea- 124, creat- 6.5, sodium- 124, Potassium-5.7
Urine routine	2+ Protein, No RBC, No WBC, No Casts
Auto-immune panel	ANA, ANCA, anti-GBM-Negative
Other investigation	LDH-500, C3 (90 mg/dl), C4 (0.2 mg/dl)-normal, viral markers negative, peripheral smear-normocytic, normochromic anemia

USG KUB showed bilateral edematous kidneys with raised bilateral echogenicity. Patient was dialyzed in view of persistent hyperkalemia and metabolic acidosis. Kidney biopsy showed severe acute tubular injury and focal interstitial nephritis. Granular stringy casts were seen in several tubular lamina. serum Total CPK was done to rule out rhabdomyolysis which was normal. patient received 4 sessions of hemodialysis during hospital stay. Gradually urine output improved and patient was discharged in stable condition. Patient attained a nadir creatinine of 0.7 at 1 month follow-up.

DISCUSSION

Traditional medicine associated renal failure is very common in African countries and China and has been infrequently reported from India.[4-7] It is very common that people In India take various herbs for losing weight, arthralgia, chronic illnesses, arthralgia, liver and kidney diseases and gynecological problem. Herbal medication use is also very common for treatment of diabetes.[8] The exact chemical composition and the proportion of various herbs in the herbal medicine is usually not known. A strong association between use of herbal medicines and interstitial nephritis is observed in many Chinese studies.[2,9] It is very difficult to diagnose kidney injury associated with herbal medicines. Diagnosis can be strongly suspected based on diachronic relationship between consumption of herbal medicines and development kidney injury and or an improvement in kidney function after discontinuation of the herbal medicines.[5,10] Herbal medications contain undisclosed drugs, such as heavy metals, vasoconstrictors, hormones, and other undeclared drugs.[3,11] Spectrum of herbal medication induced kidney diseases includes acute interstitial nephritis, acute tubular necrosis, chronic tubulointerstitial nephritis, rarely glomerular disorders and thrombotic microangiopathy.[12,13] All the above diseases have Presumptive diagnosis can be made by detailed elaborate history, basic laboratory investigations and ultrasonography. However definitive diagnosis warrants biopsy.[14] The time from presentation of the patient to histopathological diagnosis takes varied amount of time from 2 to 4 weeks. Many patients may require renal replacement therapy till final diagnosis is made and appropriate therapy is started, which creates financial stress and burden at individual level and healthcare infrastructure. Hence it becomes very important to study the safety profile of herbal medications so that early diagnosis of the illness is made in case of adverse events and timely appropriate therapy may be started. The current system of monitoring the safety of herbal medicinal products is not sufficient to collect data on all adverse effects associated with its use, which has reduced the possibility of controlling their use.[15] Extensive investigation is required to know the pharmacodynamics and pharmacokinetics of the compounds found in herbal medications. All the adverse effects following consumption of the compound should be reported.

CONCLUSION

Herbal medicine induced ATIN is a common cause of Acute kidney injury in central India which requires high suspicion and timely biopsy for detection. Early detection and stoppage of offending agent and supportive renal replacement play a vital role in reversing the injury or prevention of progressive injury. Short course of steroids

has favorable outcome in reversing interstitial nephritis.

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