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Acute oxalate nephropathy associated with herbal remedies

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ABSTRACT

The use of herbal remedies has grown in recent years, largely due to their increased production and the media advertisements which target their use for the cure of almost all symptoms. Herbal remedies have also become popular in multi-plant forms and have recently become available in both industrial and condensed formulations, with higher doses being administered. We report a 68-year-old woman presenting with symptoms of flank pain, nausea, vomiting, anuria, and hematuria. She has history diabetes mellitus, hypertension and use of herbal including *Achillea millefolium* and *Thymus migricus, Nasturtium* for the last four months. Kidney biopsy was performed and was diagnosed with oxalate nephropathy. After the use of herbals was stopped, creatinine levels returned toward normal value in the following months with no complications. Herbal remedies would cause severe organ failures if administered in high-doses and should be considered as a possible cause in patients presenting with AKI.

Implication for health policy/practice/research/medical education:
This case report presents a case with symptoms including pain, nausea, vomiting, anuria, and hematuria, as well as a history of concomitant use of multiple herbal.

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Introduction

Oxalosis is a metabolic disorder characterized by deposition in various organs, including the kidney and is divided into primary and secondary types. In its primary form, the disorder is congenital and genetic. The primary form consists of three types. The most common form of the disorder consists of mutation in alanine-glyoxylate transaminase encoding (1).

The secondary forms of hyperoxaluria may be associated with either high intestinal absorption (intestinal hyperoxaluria) or increase in internal production or the excessive consumption of oxalate. Intestinal factors comprise 5% of the reasons for hyperoxaluria, which is associated with dysfunction in fat absorption in the intestine (small intestine disease or cystic fibrosis). Unabsorbed fat in the gastrointestinal system causes a reduction in the calcium binding to oxalate and thereby the heavy absorption of oxalate. The oxalate binding to calcium is defecated through the intestine, while non-bonded oxalate is absorbed through the mucus in the large intestine (3). Vitamin B6 deficiency causes an increase in endogenous oxalate synthesis (4). Other reasons for hyperoxaluria include sarcoidosis, hyperparathyroidism (5), bariatric surgery (6) and the consumption of orlistat (7). Hyperoxalosis is one of the causes of AKI, chronic kidney disease and end-stage renal disease (2). Our patient is a 68-year-old woman with a history of diabetes and hypertension who was admitted to the emergency department with complaints of weakness, nausea and anorexia. The patient has been medication (metformin, Glibenclamide, captopril, aspirin, atorvastatin, alprazolam and Lantus insulin). She had also taken a combination of herbal medicines including *Achillea millefolium*, *Thymus migricus, Nasturtium* (genus) and *fennel seeds* for at least eight months. She complained of flank pain and dizziness over the last month and had been anuric for the past three days. On the examination, the blood pressure was 100/70 mm Hg, heart rate 100 per minute, respiration rate 26 per

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minute and body temperature 36.6°C. The patient did not show retinopathy in the eye examination. The abdominal and pelvic ultrasound results were normal. The blood gas analysis revealed metabolic acidosis (Table 1). Given her anuria and creatinine level of 9.6 mg/dL, therefore dialysis was initiated for her. Urinary sedimentation revealed hematuria with dysmorphic red blood cell, granular casts and protein 2+, then the possibility of rapidly progressive glomerulonephritis. The patient was then given three doses of 500-mg methylprednisolone.

After eight days, the patient's urine volume reached 1500 cc and the serum creatinine decreased to 2.5. Renal biopsy was conducted for the patient, which showed 25 glomeruli (Figures 1 and 2). Three of them were completely sclerotic. Some of the tubules were filled with oxalate crystals. In addition, 5-10% of the tubules were atrophic (Figure 1). The patient stopped taking herbal remedies and was discharged with the tests demonstrated in Table 2. After one month, the patient's serum creatinine decreased to 1.3 mg/dL.

Table 1. Laboratory test data upon hospital admission

Variable	Result	Unit	Reference range
Blood count			
Leukocytes	9.80	10^3µL	3.5-10.5
Erythrocytes	39	10^6 µL	4.3-6.1
Hemoglobin	10	g/dL	13/5-17.5
Hematocrit	30.3	%	36-46 (%)
Platelet	320	10^3	145-420
Chemistry			
FBS	210	mg/dL	70-100
Urea	190	mg/dL	10-50
creatinine	6.9	mg/d	0.6-1.2
Uric acid	8.1	mg/dL	3.6-7.5
Sodium	138	meq/L	35-145
Potassium	4.8	meq/L	3.5-4.5
Calcium	7.3	mgq/L	8.5-10.5
Phosphorus	6.8	mg/dL	2.9-5
C-reactive protein	2+		
ESR	45	mm/h	0-15
Urinalysis			
White cells	10-12		
pH	5.0		
Protein	2+		
Glucose	2+		
Blood	30-40		
SG	1016		
Sediment			
WBC	10-15 WBC cast many		
Red cells	20-30 RBC and dysmorphic		
Epithelial cells	2-3		
Granulated casts	3-5		
Immunology			
Protein electrophoresis	Normal		
C3	92	Normal	
C4	65	Normal	
ANA	4	Negative	
ANCA- P	7	Negative	
ANCA-C	9	Negative	
Anti GBM		Negative	
HBS Antigen		Negative	
HCV Ab		Negative	
HIV Ab		Negative	

Discussion

In traditional medicine, herbal remedies have many applications, including in diabetes (10), hypertension (8,9), weight loss (11), kidney stones (12) and hypercholesterolemia (13). Unfortunately, occasionally prescription of multiple herbal remedies at the same time. Some of these herbal remedies have high oxalate levels and their availability in concentrate forms means the delivery of higher doses of oxalate to the body, which can even lead to fatalities. In one study, Holmes et al found that administration of approximately one gram of oxalate daily to a healthy person does not cause acute oxalate nephropathy (14). The minimum lethal dose of oxalate in adults is 4-5 grams (15). The patient in the present case report concomitantly consumed *A. millefolium* and *T. migricus* for hypertension and diabetes. In a study by James Hong et al 100 mg of *A. millefolium* was found to contain 1332 mg of oxalate, only 423 mg of which is solvent and *T. migricus* was found to have 245 mg of oxalate, with 167 mg being solvent (16).

After excluding the secondary causes of oxalate nephropathy, the use of herbal medicines seems to be the cause of oxalate nephropathy in our patient and after cessation of herbal medicines, the kidney functions ameliorated.

Table 2. Laboratory test data at discharge

Variable	Result	Unit	Reference range
Blood count			
Leukocytes	8.80	10^3µL	3.5-10.5
Erythrocytes	30	10^6 µL	4.3-6.1
Hemoglobin	10.2	g/dL	13/5-17.5
Hematocrit	30.5	%	36-46 (%)
Platelet	220	10^3	145-420
Chemistry			
FBS	140	mg/dL	70-100
Urea	68	mg/dL	10-50
Creatinine	2.5	mg/d	0.6-1.2
Uric acid	6.1	mg/dL	3.6-7.5
Sodium	149	mEq/L	35-145
Potassium	3.8	mEq/L	3.5-4.5
Calcium	9.3	mg/dL	8.5-10.5
Phosphorus	5.8	mg/dL	2.9-5
C-reactive protein	2+		
ESR	25	mm/h	0-15

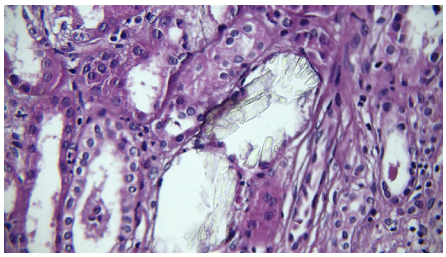

Figure 1. High power magnification of renal biopsy showing tubule with oxalate crystal associated with tubular injury represented by flattened epithelium

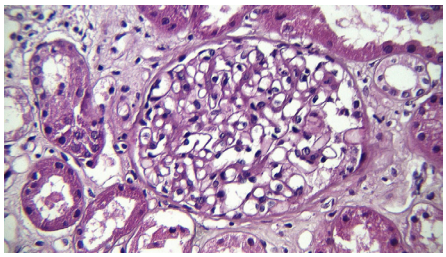

Figure 2. The glomerulus shows no obvious changes. There is some mesangial expansion and no thickening of glomerular basement membrane

Conclusion

Herbal remedies are not free of side effects and patients should be trained to inform their physician of the herbal remedies they are taking.

Authors' contribution

Case management and handling by BB. Pathology report by MA. Both authors read and signed the final paper.

Conflicts of interest

The authors declare that they have no competing interests.

Ethical issues

Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors. This case report was conducted in accord with the World Medical Association Declaration of Helsinki. Written informed consent was obtained from the patient for publication of this report.

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