

CASE REPORT**A case report of chronic interstitial nephritis associated with Chinese herbal supplement Zi Xiu Tang Bee Pollen****Hiren J. Joshi, Reginald Obi**

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Correspondence: Reginald Obi. Address: 2355 West Arlington Boulevard, Greenville, NC 27834, USA. Email: obir@ecu.edu**Received:** February 23, 2014**Accepted:** March 25, 2014**Online Published:** March 28, 2014**DOI:** 10.5430/crim.v1n2p65**URL:** <http://dx.doi.org/10.5430/crim.v1n2p65>**Abstract**

We report a case of renal failure associated with ingestion of Chinese herbal weight loss supplement called Zi Xiu Tang Bee Pollen. A 33 year old African American female who had been ingesting Zi Xiu Tang Bee Pollen for about one year in duration. The patient presented to our facility with renal failure requiring dialysis for one month from unknown etiology. The patient had a normal creatinine level a few months prior to starting dialysis. The patient had no additional medical history. Her urine studies were positive for sterile pyuria, suggestive of interstitial nephritis. She subsequently underwent a kidney biopsy which showed severe chronic interstitial nephritis due to Zi Xiu Tang Bee Pollen. The Chinese herbal supplement was discontinued, but patient remained dialysis dependent. Our literature search showed one other reported case of bee pollen associated with acute interstitial nephritis that required short term hemodialysis with renal recovery after discontinuation of supplement. This unique case highlights the growing health risks posed by nonprescription diet supplements and they can potentially add to the increasing burden of kidney disease.

Keywords

Chronic interstitial nephritis, Chinese herbal nephropathy

1 Introduction

There is growing use of herbal supplements in the US ^[1]. In 1990, 2.5% of the US population used one or more herbal products ^[2]. In 2002 nearly 1 in 5 people in the US population report using an herb for treatment of health conditions and/or health promotion and more than half did not disclose this information to a conventional medical professional ^[3-6]. These herbal remedies are readily available without FDA approval because they are marketed as dietary supplements. Zi Xiu Tang Bee Pollen, a Chinese herbal supplement is marketed as weight loss and body reshaping supplement. It contains over eighteen ingredients touted as naturally occurring. A 2010 FDA investigation found hidden drug ingredients in particular Sibutramine ^[7]. Sibutramine is a controlled substance once marketed in the popular weight loss pill Meridia. Meridia was withdrawn from the market due to adverse cardiac effects such as high blood pressure, tachycardia, and both arrhythmias and congestive heart failure in patients with coronary artery disease ^[8]. During pre-marketing studies of Meridia one published case of biopsy confirmed acute interstitial nephritis was reported ^[9]. It is unlikely that anyone knows exactly the extent of nephrotoxicity associated with these herbal supplements as we are left with mostly case reports to make inferences from. We are aware of one such case of acute interstitial nephritis with bee pollen supplement ingestion in the

literature that required discontinuation of the supplement and short term hemodialysis with eventual renal recovery [10]. Here we present a second case but unlike the first one this patient has remained dialysis dependent.

2 Case report

A thirty three-year-old African American female presented to our hospital for evaluation of chest pain. She was recently declared ESRD and started on hemodialysis just one month prior but the exact etiology of her kidney disease was unclear. Patient was admitted at an outside hospital one month prior for acute renal failure and found to be uremic requiring urgent dialysis and has remained on dialysis since. She has a past medical history significant for obesity, asthma, anxiety, depression, and recurrent asymptomatic urinary tract infections noted within the last year on urine dipsticks during routine health care visits but with negative urine cultures. She did not have any family history of kidney disease. She does not smoke or drink alcohol and no history of substance abuse. She denied using frequent NSAIDs, no blood in urine or recent diarrhea, no cough, sore-throat or sick contact. On further questioning at our facility she provided an added history of using a Chinese herbal supplement called Zi Xiu Tang Bee pollen for weight loss. She had been using this supplement for about one year and was still using this even after dialysis initiation.

3 Clinical findings

She did not have any rash, joint swelling, oral ulcers, pharyngeal exudates, lymphadenopathy, and negative ophthalmic findings. She had a recent creatinine of 0.95mg/dL about 3 months prior to her dialysis initiation. On imaging study her renal ultrasound showed moderately echogenic kidneys bilaterally, right kidney measuring 12cm and left kidney measuring 11cm in length. Her chest x-ray showed no acute pulmonary processes. She had multiple urinalysis that showed pyuria and microscopic hematuria but her urine cultures were negative. She had subnephrotic range proteinuria of 2.1g on a spot urine protein to creatinine ratio. Her renal biopsy showed severe chronic interstitial nephritis with some secondary focal and segmental glomerular scarring. There were no immune complex deposits on her immunofluorescence stains.

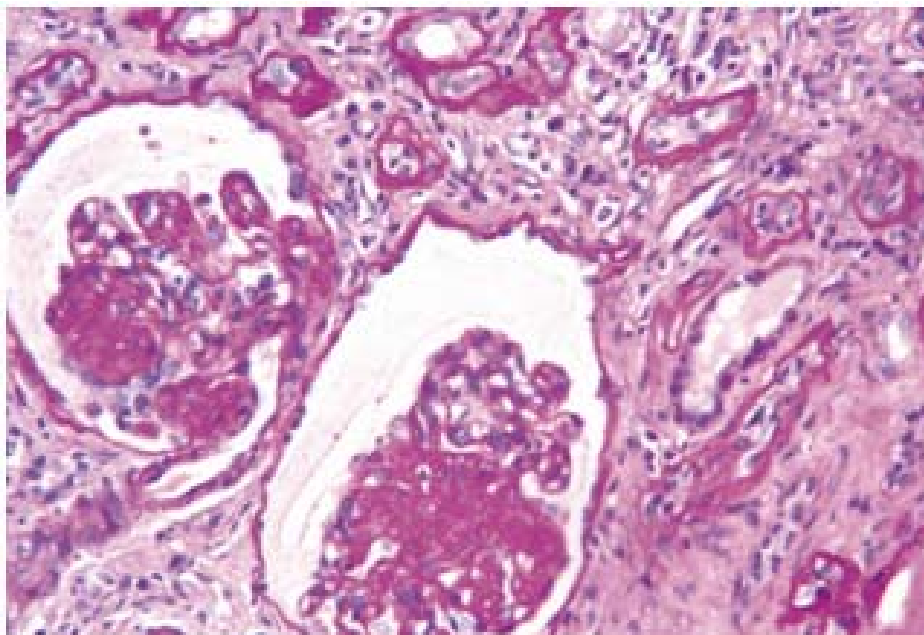


Figure 1. Global and segmental glomerulosclerosis.

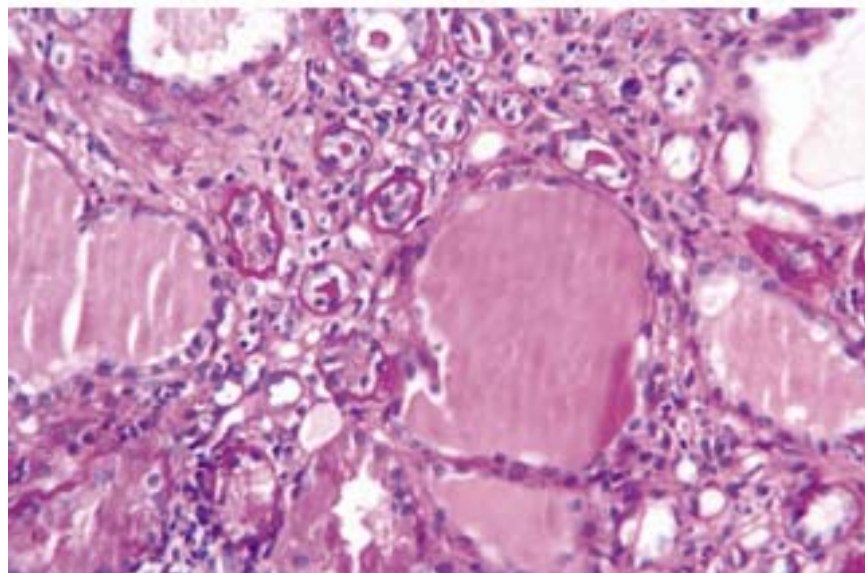


Figure 2. Tubular atrophy, interstitial fibrosis mononuclear inflammation

Table 1. Clinical findings on admission

Variables	Normal Range	Result	Unit
Complete blood count			
Hemoglobin	12-16	9.4	g/dL
Hematocrit	35-47	29.7	%
White blood cell	4.5-11	11	k/uL
Neutrophil	1.8-7.7	8.8	k/uL
Monocytes	0.0-0.8	0.6	k/uL
Eosinophil	0.0-0.5	0.1	k/uL
Platelet count	150-440	227	k/uL
Chemistry			
Sodium	135-145	138	mEq/L
Potassium	3.5-5.0	5.1	mEq/L
Chloride	99-109	112	mEq/L
Bicarbonate	22-33	15	mEq/L
Blood urea nitrogen	6-20	39	mg/dL
Creatinine	0.6-1.10	5.36	mg/dL
Glucose	70-105	123	mg/dL
Calcium	8.5-10.5	8.9	mg/dL
AST	10-31	14	U/L
ALT	10-41	11	U/L
ALP	41-120	113	U/L
Total Protein	6.2-8.3	8.1	g/dL
Albumin	3.4-4.1	3.7	g/dL
Complement			
C3	84-160	175	mg/dL
C4	12-36	54	mg/dL
Autoimmune Studies			
ANA		<40	

(Table continued on page 68)

Table 1. (continued.)

Anti-DNA Antibody	Negative	
Glomerular Membrane Antibody	< 1.0 (not detected)	
Cardiolipin Antibody	< 14 (neg)	
Cryoglobulin	Negative	
RPR	Non-reactive	
Hep B-Serology	Negative	
Hep A Ab-IgM	Negative	
Hep C Ab	Negative	
Urinalysis		
Protein	3+	Urine prot/cr ratio-2.1
RBC	20-50	
Leukocyte Esterase	2+	Urine eosinophil- Neg
WBC	20-50	
Nitrite	Negative	
Urine Culture	<100K CFU/mL Mixed Flora	

4 Discussion

Drugs and toxins account for a significant cause of chronic tubulointerstitial nephritis. The degree and chronicity usually determines the extent of the resulting renal damage. Our case illustrates once again the risk posed by herbal weight loss supplements. Our patient had been using this weight loss supplement for her obesity for about one year in duration and since she considered it to be “natural occurring supplement” rather than a drug, she failed to mention this in her list of home meds. She had been treated multiple times for presumed urinary tract infection based on the finding of pyuria on urinalysis; however her urine cultures had been negative to mixed flora. After reviewing laboratory studies, she had interstitial nephritis all along most likely from her chronic ingestion of Zi Xiu Tang Bee Pollen. There are no specific clinical symptoms and signs associated with drug induced chronic interstitial nephritis. Our patient was mostly asymptomatic and hence the delay in diagnosis with the resulting consequence of severe chronic kidney failure.

Several drugs are known to cause interstitial nephritis however in many cases trying to ascertain causality can be difficult especially with patients who are on multiple medications at a time. Fortunately our patient was not on any chronic medication known to cause allergic interstitial nephritis. Her only chronic medication was Zi Xiu Tang Bee Pollen, making this the likely culprit for her renal disease.

We are aware in the literature of one other case of acute interstitial nephritis with Bee pollen reported in Japan^[10]. In that case report the patient recovered with discontinuation of the supplement but was left with residual stage II chronic kidney disease. With so many ingredients blended in this herbal supplement (including hidden ones) we cannot speculate on the exact ingredient(s) responsible for this patient’s renal toxicity.

Chinese herbal nephropathy have become synonymous with Aristolochic acid nephropathy. It is a worldwide problem whose actual incidence is unknown and likely underestimated^[11]. Vanherweghem et al reported the original case series of patients in Brussels with rapidly fibrosing interstitial nephritis after using Chinese weight loss supplements due to aristolochic acid^[12]. In their analysis of those supplements they found alkaloid-like material in the capsules taken by the patients but not in the samples of the Chinese powders provided by the import company casting serious doubt on the actual components of these supplements. Lai et al in a study done in Taiwan highlighted the risk of kidney failure due to aristolochic acid consumption in herbal products containing Mu Tong or Fangchi^[13]. Yang et al reported rapidly

progressive fibrosing interstitial nephritis with Chinese herbal drugs^[14]. Their study also showed that renal function deterioration continued in most patients despite discontinuation of the herbal medications.

The exact mechanism(s) of renal injury leading to Chinese herb nephropathy is unclear. Support for Aristolochic acid induced nephropathy have come mostly from animal models of injury in rabbit's, rat and mice^[15]. One study linked certain cell signaling pathways with mediating the characteristic cell death and severe tubular fibrosis associated with this nephropathy implicating TGF-beta/Smad 3 pathways^[16]. Another suggests that aristolochic acid induces tubular epithelial cell death via apoptosis by dephosphorylation of STAT3 and posttranslational activation of P53, to promote renal injury and nephropathy^[17]. Also implicated is DNA adduct formation and decreased megalin expression and inhibition of receptor mediated endocytosis of low molecular weight proteins^[18]. Other possibly important factors include toxin dose, batch-to-batch variability in toxin content, individual differences in toxin metabolism, and a genetically determined predisposition toward nephrotoxicity and/or carcinogenesis^[19].

Conclusion

There continues to be a growing trend in the use of herbal supplement for weight loss amongst other medicinal indications. However their safety remains a concern. The finding of hidden ingredient Sibutramine in Zi Xiu tang Bee Pollen by the FDA raises serious questions about its other constituents and possible health risks in particular nephrotoxicity. Creating awareness to these risks and promoting more public discussion is warranted.

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