

Prevention of Renal Damage by Treating Hyperuricemia

Azar Nickavar

Department of Pediatric Nephrology, Aliasghar Children Hospital, Iran University of Medical Sciences, Tehran, Iran

Correspondence to:

Dr. Azar Nickavar,
Aliasghar Children Hospital, Iran
University of Medical Sciences.
E-mail: anickavar@yahoo.com

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ABSTRACT

Nephrolithiasis, obstructive renal failure, essential hypertension, and chronic tubulointerstitial nephritis have been considered as the renal complications of hyperuricemia. Massive proteinuria has been rarely reported as the primary manifestation of increased serum uric acid. This is the report of a child presented with proteinuria, hypertension, and glomerular sclerosis secondary to hypouricosuric hyperuricemia, who was treated by uric acid lowering management.

Keywords: Glomerular sclerosis, hypertension, hyperuricemia, proteinuria

INTRODUCTION

Uric acid is the end product of human purine metabolism. Increased serum uric acid has been considered with different metabolic, cardiovascular, and renal disorders.^[1]

Glomerular, tubulointerstitial, and vascular involvement^[2] with eventual chronic renal disease has been reported in hyperuricemia.^[3,4] Recognition of the different manifestations and complications of hyperuricemia seems beneficial to prevent renal damage in the early phase.

CASE REPORT

A 2 year and 9 months girl was admitted for seizure, severe hypertension (200/110), and renal failure. She had a previous admission in another hospital for isolated proteinuria, with no clinical follow-up. Family history was negative for any previous renal disease.

Laboratory exams [Table 1] revealed hyperuricemia (uric acid: 18 mg/dl), increased serum creatinine, microscopic hematuria, and nephrotic syndrome. Liver function tests, serum catecholamines, LDH, vitamin B12, and complement level, were normal. ANA, anti-dsDNA, ANCA, anti-GBM, rubella, CMV and HCV antibody, BK virus, HBS ag, and urine MPS were all negative. Serum level of renin and aldestrone was elevated. Decreased urinary excretion with increased serum level of uric acid (hypouricosuric hyperuricemia) confirmed by excluding all other causes of hyperuricemia. Normal to mild renal enlargement with bilateral increased echogenicity and increased resistive index

in favor of parenchymal renal disease with no renal stenosis detected in ultrasound exam. Voiding cystourethrography was normal. Severe diastolic dysfunction with concentric left ventricular hypertrophy and decreased ejection fraction in favor of chronic hypertension were documented in echocardiography.

Peritoneal dialysis was performed for acute renal failure in addition to antihypertensive treatment. Renal biopsy showed diffuse global sclerosis with glomerular hypertrophy, increased mesangial cellularity, segmental solidification, tubular atrophy, focal inflammation, and arterial narrowing with the impression of ESRD and end arteritis fibrosa, suggested the possible changes of chronic malignant hypertension superimposed on focal segmental glomerulosclerosis [Figure 1]. Immunofluorescence study was negative.

Despite of improved renal function (serum creatinine: 0.8 mg/dl), serum uric acid was persistently elevated in repeated samples with

low urine uric acid. A second renal biopsy performed for disproportional improved renal function compared to distorted renal biopsy revealed segmental and global glomerular sclerosis, mild to moderate hyperplasia in small arterioles and chronic inflammation with interstitial fibrosis [Figure 2]. Therefore, the first renal biopsy assumed to be taken from a nidus of glomerular sclerosis. As a primary focal segmental glomerular sclerosis, she was treated with corticosteroids followed by conventional immunosuppressive treatments (cyclosporine, mycophenolate mofetile), with no clinical response. But, proteinuria decreased significantly by uric acid lowering agents. Genetic analysis revealed no documented mutation for common NPHS2 gene mutation. During the follow-up period on allopurinole and anti-proteinuric treatment, the patient had normal renal function with mild to moderate proteinuria and no recurrence of nephrotic syndrome.

Table 1: Laboratory variables at presentation and post treatment

Variables	Values
Renin	>500 pg/dl
Aldosterone	>2000 pg/dl
Initial creatinine	3.2 mg/dl
Next creatinine	0.8 mg.dl
Initial uric acid	18 mg/dl
Initial urine prot/creat	>2
Next urine prot/creat	<1
Initial urine uric acid/creat	>1

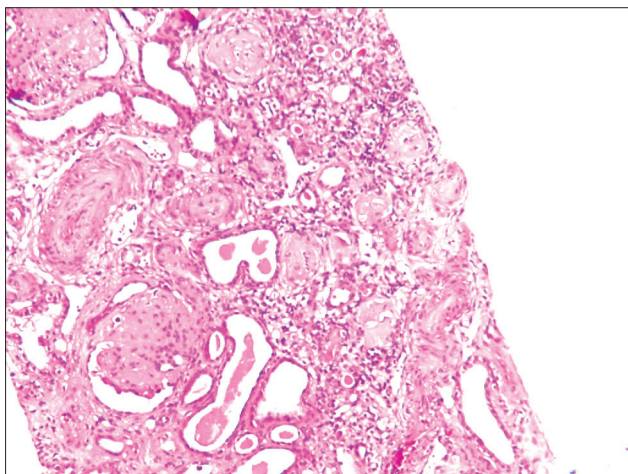


Figure 1: Diffuse global glomeruli sclerosis (×400, PAS stain)

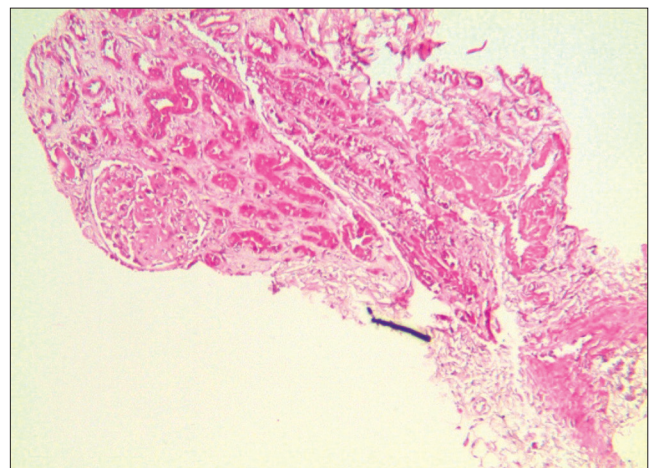


Figure 2: Segmental sclerosis in one glomerule (×400, PAS stain)

syndrome, GSD type 1, sarcoidosis, and drug administration.^[5,6] Familial juvenile hyperuricemic nephropathy is an inherited disorder characterized by hypouricosuric hyperuricemia, progressive tubulointerstitial nephritis, and chronic renal failure and is considered as the possible underlying disease in this patient.^[7]

Nephrolithiasis is the most common renal involvement in hyperuricemia, complicated by acute obstructive renal failure.^[3]

A pathogenic link has been reported between hyperuricemia and essential hypertension through activation of renin-angiotensin system, downregulation of nitric oxide, vascular muscle proliferation, afferent arteriolosclerosis, altered pressure natriuresis, endothelial dysfunction, and abnormal cellular sodium transport.^[8-10] Lowering uric acid level controls hypertension in some patients initially,^[9] becomes irreversible, salt sensitive, and resistant to uric acid lowering treatment later.^[11]

In addition, moderate degrees of asymptomatic hyperuricemia are not injurious to the kidney.^[6] But, interstitial damage occurs more commonly in hyperuricemic gout.^[12] Glomerular hypertrophy/hypertension, afferent arteriolar sclerosis, and macrophage infiltration,^[4] vasoconstriction, chronic ischemia, morphologic changes similar to focal mesangio-capillary or mesangial proliferative glomerulonephritis with increased mesangial cells and matrix, focal segmental glomerular sclerosis, capillary basement membrane thickening, and chronic tubulointerstitial damage progressive to end-stage kidney disease have been reported in chronic hyperuricemia.^[13-15]

This patient had persistent proteinuria originated from glomerular sclerotic lesions secondary to chronic hypouricosuric hyperuricemia. Proteinuria decreased significantly by uric acid lowering agents and antiproteinuric treatment. Therefore, measurement of serum uric acid and early treatment of hyperuricemia are recommended in patients with idiopathic proteinuria to prevent further renal damage.

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