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Original Article

Hyperuricemia as a marker for progression of immunoglobulin A nephropathy

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Abstract

Background: The variable clinical and histopathological manifestations of immunoglobulin A nephropathy (IgAN) make it difficult to predict disease progression. A recent study showed that hyperuricemia, a condition common in hypertension and vascular disease, may contribute to renal dysfunction and histological changes including renal arteriosclerosis, tubular atrophy, and interstitial fibrosis. Herein, we investigated the clinical significance of uric acid level at the time of biopsy, as a marker of IgAN progression.

Methods: We included 193 patients with biopsy-proven IgAN. Renal disease progression was defined as serum creatinine elevation above 1.2 mg/dL or over 20% elevation from baseline. Hyperuricemia was defined as a serum uric acid level $\geq$ 7.3 mg/dL in men and $\geq$ 5.3 mg/dL in women, which were 1 standard deviation above the mean value in the normal subjects.

Results: The hyperuricemia group (n=50) had higher blood pressure, body mass index, and serum creatinine, and a greater amount of proteinuria and a lower glomerular filtration rate than the nonhyperuricemia group (n=143). Hyperuricemia increased the risk of IgAN progression (odds ratio, 4.53; 95% confidence interval, 1.31–15.66). The disease progression group (n=26) had a greater frequency of hyperuricemia, hypertension, and nephrotic range proteinuria than the nonprogression group (n=119). The renal survival analysis showed that the hyperuricemia group had a higher rate of IgAN disease progression.

Conclusion: Hyperuricemia at the time of diagnosis is an important marker for IgAN progression.

Introduction

Immunoglobulin A nephropathy (IgAN) is the most common chronic glomerulonephritis worldwide [1]. The course of IgAN is variable, with 10%–20% of patients developing end-stage renal disease in the first 10 years after the diagnosis [2]. Early detection and intervention for adjustable risk factors may reduce or slow the rate of progression of chronic renal

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disease. The risk factors associated with poor prognosis are renal insufficiency, hypertension, and proteinuria at the time of diagnosis [3]. Recent studies suggest that uric acid is associated with IgAN progression [4,5].

High serum uric acid levels may reflect a decrease in renal blood flow and early hypertensive nephrosclerosis. Serum uric acid may play a pathologic role in renal vasoconstriction, endothelial dysfunction, inflammatory response, oxidative stress, and the disturbances in autoregulation that occur with acute renal failure [6]. Recently, the reassessment of the role of hyperuricemia suggests its direct pathogenicity as well as a marker for other associated risk factors [7–10].

The aim of the present study was to evaluate the association between uric acid levels at the time of IgAN diagnosis and renal prognosis in patients with biopsy-proven IgAN.

Methods

Study population and study design

This study included all the patients with IgAN diagnosed at the Soonchunhyang University Cheonan Hospital between January 1999 and December 2005. A renal biopsy specimen was considered adequate if it contained 4 or more glomeruli. IgAN was defined as glomerulonephritis with predominant IgA deposition in the glomerular mesangium. 193 patients (103 men [53.4%] and 90 women [46.6%]) fulfilled this criterion. The median age at the time of renal biopsy was 34 years (range 14–71). The Hospital's Investigational Review Board approved this study and all participants provided written informed consent. The clinical data were collected by retrospective review of the medical record system of the Hospital.

Clinical data

Systemic lupus erythematosus, liver cirrhosis, or the typical picture of Henoch–Schönlein purpura was not observed in our cases. Of the 193 patients (hyperuricemia, $n=50$; nonhyperuricemia, $n=143$) enrolled in the study at the time of renal biopsy, 48 (24.9%) were excluded: 33 did not attend follow-up visits, 13 had incomplete laboratory data, and 2 were followed for <1 year. Thus, 145 patients were included in the analysis (hyperuricemia, $n=37$; nonhyperuricemia, $n=108$; Fig. 1). The median follow-up time after renal biopsy was 5.8 years (range 1.2–10). All the clinical parameters were measured at the time of renal biopsy. Data on medication, diabetes mellitus, body mass index (BMI), blood pressure (BP), 24-h urinary protein excretion, serum lipid profile, and serum uric acid level at the time of renal biopsy were recorded. The definition of hypertension was the use of antihypertensive medication at the time of renal biopsy or a systolic BP >140 mmHg and/or diastolic BP >90 mmHg as measured during hospitalization for renal biopsy. By this definition, 40 patients had hypertension. Nine patients had diabetes mellitus (non–insulin-dependent diabetes mellitus). The pathology grading system was determined according to Lee [11]. Hypercholesterolemia and hypertriglyceridemia were defined as serum cholesterol >250 mg/dL and serum triglyceride >200 mg/dL, respectively.

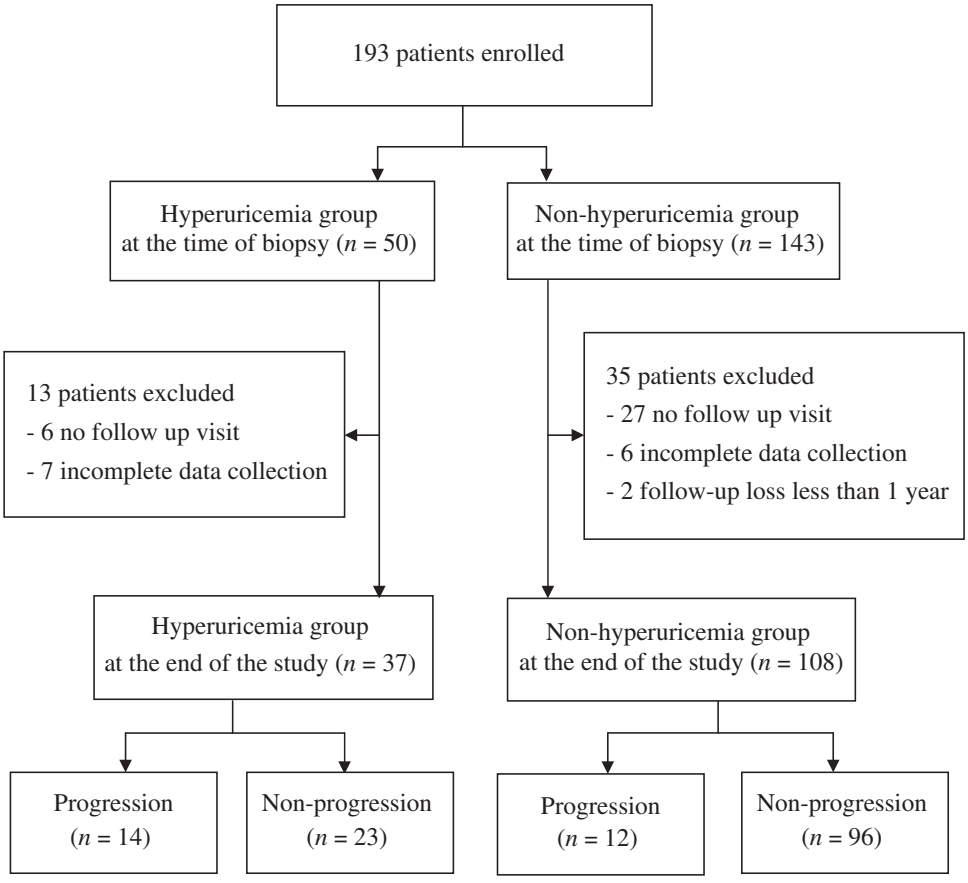

Figure 1. Study design and renal outcomes.