Frequent Abnormalities of Renal Function in Patients with Rheumatoid Arthritis

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Dear Sir,

Subclinical renal dysfunction has been reported in patients with rheumatoid arthritis (RA) [1, 2]. Some studies provided evidence that nephropathies are the result of both a long-term treatment with antirheumatic drugs (nonsteroidal anti-inflammatory/analgesic drugs, parenteral gold, D-penicillamine), and complications of RA (amyloidosis) [3, 4].

The purpose of this study was to evaluate the frequency and the severity of renal dysfunction in patients with RA, using sensitive tests of glomerular and tubular function. Fifty-two consecutive patients with seropositive RA, followed at the outpatient clinics, Rheumatology Division, Escola Paulista de Medicina, during the year of 1990, were evaluated in a cross-sectional study. Exclusion criteria were: diabetes mellitus, urinary tract infection, urolithiasis and severe hypertension. All subjects were taking nonsteroidal anti-inflammatory drugs, mainly indomethacin, ibuprofen, ketoprofen and naproxen; 4 were taking parenteral gold, 2 received D-penicillamine, and 1 was taking sulfasalazine. No patient had diagnosis of secondary amyloidosis. The following variables were measured: count and morphology of hematuria, microalbuminuria was determined by enzyme-linked immunosorbent assay (ELISA) [5], urinary excretion of β_2 -microglobulin β_2 M [6], and urinary retinol-binding protein (RBP) by ELISA [7]. Creatinine and ⁵¹Cr-EDTA clearances [8] correspond to the mean value of three consecutive 1-hour period samples. Urinary β_2 M, RBP and microalbuminuria were related to the creatinine concentration in the same sample. For microalbuminuria,

Table 1. Renal function tests in RA patients

Test
Patients

Median
Range

n
%

Creatinine clearance, ml/min/1.73 m²

96

51–156

< 80 ml/min

12/47

26

⁵¹Cr-EDTA clearance, ml/min/1.73 m²

104

74–149

< 80 ml/min

3/10

30

Dysmorphic hematuria³

21/52

40

Albuminuria, mg/g creatinine

4.7

0.6–28.5

above normal^b

2/42

5

Urinary β₂M, μg/g creatinine

78

16–703

above normal⁰

16/42

38

Fractional excretion of β_2 M, %

0.03

0.01–0.25

above normal

12/33

36

Urinary RBP, μ g/g creatinine

85

10–811

above normal

11/30

37

> 10 red blood cells/high power field; upper normal levels; 13.8 mg/g creatinine; 105 μ g/g creatinine; 0.03%; 103 μ g/g creatinine.

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urinary β_2 M and RBP, the upper limit of normal was defined as the mean + 2 SD of the urinary concentrations observed in a group of healthy subjects.

The mean age of the patients was 54 years (range 22–78), 41 were females and 11 males. Median duration of RA was 8.0 years (1–30). Decreased creatinine clearance (< 80 ml/min/1.73 m²) was found in 12/47 (26%) patients; dysmorphic hematuria: 21/52 (40%); increased microalbuminuria: 2/42 (5%); increased urinary β_2 M: 16/42 (38%); increased fractional excretion of β_2 M: 12/33 (36%), and elevated urinary RBP: 11/30 (37%) (table 1). There were significant correlations (Spearman's coefficient) between urinary RBP and β_2 M ($r = 0.52$, $p = 0.02$), β_2 M and albuminuria ($r = 0.58$, $p < 0.001$), RBP and albuminuria ($r = 0.41$, $p = 0.02$), hematuria and β_2 M ($r = 0.47$, $p < 0.001$), hematuria and RBP ($r = 0.47$, $p < 0.01$), hematuria and albuminuria ($r = 0.58$, $p < 0.001$), duration of RA and excretion of β_2 M ($r = 0.53$, $p = 0.002$), duration of RA and RBP ($r = 0.54$, $p < 0.001$), duration of RA and hematuria ($r = 0.43$, $p < 0.01$). Based on these results we conclude that subclinical renal damage, as shown by sensitive tests of glomerular and tubular function, is frequent in patients with RA, particularly in those with long-standing disease. These dysfunctions are probably associated with the long-term drug treatment for RA. Patients who present abnormalities indicated by these early markers of renal dysfunction should be under close monitoring of renal function, specially if they need to receive nephrotoxic drugs (nonsteroidal anti-inflammatory drugs, gold, E>-penicillamine, cyclosporin, antibiotics,

etc.). Prospective studies seem justified to clarify the long-term significance of these subclinical renal dysfunctions in RA patients.

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