CLINICAL, BIOCHEMICAL AND HISTOPATHOLOGICAL FINDINGS AND LONG-TERM PROGNOSIS IN MESANGIOCAPILLARY GLOMERULONEPHRITIS

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SUMMARY: In this study, three years follow-up of 26 patients with mesangiocapillary glomerulonephritis (MCGN) was assessed. First group consisted of 15 patients (mean age 30.0±13.6); whose proteinuria became negative and serum creatinine levels dropped below 2 mg/dl at the end of 3 years. Group II included 11 patients whose proteinuria continued and renal functions did not improve or deteriorated (Mean age 23.2±8.8). In three patients of group II end-stage renal disease developed in 6th, 12th and 24th months and the remaining patients of this group showed decreased renal function and/or continued proteinuria. During the first assessment in Groups I and II, the rate of nephrotic syndrome 60% (9/19) and 72% (8/11), hypertension 53% (8/15) and 63% (7/11) was noticed.

In preliminary evaluation the prognostic factors were the presence on renal biopsies of tubulointerstitial changes (TIC) (27% and 80% groups I and II), vascular involvement (18.2% and 90% Groups I and II), glomerulosclerosis (9.1% and 60%). In the group II with poor prognosis creatinine clearance (Ccr) was lower and leukocyte count was higher compared to group I, whereas statistically significant differences were not found.

As a result; Among our 26 patients with MCGN the complete recovery from disease was 57.6%, and the factors which influenced the prognosis at the beginning of the process were renal biopsy findings including the presence of glomerulosclerosis, vascular involvement (VI) and tubulointerstitial changes (TIC), rather than biochemical and clinical signs.

Key Words: Mesangiocapillary glomerulonephritis, tubulointerstitial changes, glomerulosclerosis.

INTRODUCTION

Studies on the long term course of MCGN, due to rarity of the disease have previously been carried out only on small numbers of cases (4). The prognosis is generally considered unfavorable (4), but there still is uncertainty about the factors causing the deterioration to end stage renal failure or even death (7). We noticed certain correlations between the severity of tubulointerstitial changes on the biopsy and renal function in MCGN. Therefore we are interested in determining whether these changes as well as the clinical, biochemical and histopathological parameters and treatment regimens are of prognostic significance.

PATIENTS AND METHODS

Twenty-six patients (9 males, 17 females) with MCGN were weighed-up during the 36 months period between 1986-1991 in our department.

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Findings of physical examination, hematocrit (hct), white blood cell (WBC/mm^3) count, ESR (by the westergreen method, mm/hours), urine sediment, daily proteinuria (by the Esbach method, gr/day), serum albumin levels (gr/dl), total lipid (mg/dl), cholesterol (mg/dl), serum creatinine (mg/dl), corrected Ccr (ml/minute/1.73 m^2) levels were considered by the routine laboratory tests on admission. All of the parameters were repeated in the 6th, 12th, 24th and 36th months. The patients whose serum creatinine was less than 2 mg/dl and negative urinary protein were consisted as group I. In group II, the patients have disordered renal functions and/or continuous proteinuria during the control period.

Table 1: Clinical, laboratory and histopathological findings of the patients on first admission.

	Group I	Group II
Patient Age (Years)	30.0±13.6	23.2±8.8
Duration of Disease (month)	17.7±19.2	19.3±15.3
Nephrotic Syndrome	%60.0	%72.0
Hypertension	%53.3	%63.6
Hematuria	%86.6	%72.0
Silendiruria	%66.6	%63.6
Tubulointerstitial Changes	%27.2	%80.0
Vascular Involving	%18.2	%90.0
Glomerular Sclerosis	%9.1	%60.0

By the American Heart Association data, hypertension was considered if the mean blood pressure (MBP) was more than 105 mm/Hg.

Nephrotic syndrome was defined as the association of proteinuria (>3.5 gr/day), hypoalbuminemia (<3 gr/dl), edema and hyperlipemia.

Percutaneous renal biopsy was performed on patients. Biopsy data of 5 patients (4 patients in group I, 1 patient in group II) were not presented in our center, because renal biopsies were performed other hospitals, their reports however were available. Renal biopsy specimens were examined on light microscopy. On the renal biopsy specimens; tubular atrophy, interstitial fibrosis and interstitial atrophy were named tubulointerstitial changes; thickening of vascular wall, fibrinoid degeneration, fibrinoid necrosis and endothelial irregularity were named as vascular wall involving. Prednisolone (1 mg/kg/day), dypridamol (225 mg/day) and cyclophosphamide (2 mg/kg/day) were given to the patients. The drug doses were regulated, considering the renal function tests, proteinuria and WBC count during each control period.

Statistical analysis of data was performed using Student's t test.

RESULTS

There were 26 patients in this study. The baseline clinical, laboratory and histopathological findings of the patients are seen in Tables 1 and 2.

As can be seen in Tables 1 and 2, clinical and laboratory findings were not different between group I and group II, on first admission. Histopathological findings however, were naturally different.

Only one of the patients had glomerular sclerosis (9.1%) on renal biopsies in group I, and of the patients 6 had glomerular sclerosis (60%) in group II. Tubulointerstitial changes and vascular involving ratios were 27.2% and 18.2% in group I, 80.0% and 90.0% in group II respectively.

Mean blood pressure of the patients who had tubulointerstitial changes was higher than that of the patients who had no tubulointerstitial changes in Group ($p>0.05$). Also, MBP of the patients who had vascular involving was higher than the patients who had no vascular involviellent. But this finding was not statistically significant ($p=0.5$). In group II, baseline Ccr levels of the patients who had no tubulointerstitial changes were higher than the patients who had developed tubulointerstitial changes on renal biopsies (Table 3).

After therapy, serum levels of total lipids and cholesterol were improved in the 24th month, serum albumin levels were improved in the 12th month, proteinuria and ESR levels were improved in the 6th month in group I. All of them were statistically significant according to the pretreatment levels. White blood cell counts of pre and post treatment periods remained unchanged.

In group II, only Ccr levels were lower in the 36th month or the therapy according to first admission level and it was statistically significant ($p<0.05$). There were no significant differences among other laboratory and clinical data of pre and post-treatment evaluations ($p=0.5$) (Table 2).

Even to the end of 36th months of therapy, in 15 patients (57.6%) complete remission was developed but in 11 patients (42%) disordered renal function and proteinuria had been noticed. In three patients of group

II, ESR developed within the 6th, 12th and 24th months and the other patients at the end of 3 years of therapy showed the mean of Ccr 38.0±16.6 ml/min (Range : 9-54 ml/min/1.73m^2) and proteinuria 4.2±1.2 g/day (Range : 2.5-6 g/day).

DISCUSSION

Patients with MCGN can be seen with different clinical findings as reported by Cameron (3), Habib *et al.* (6). Kim and Michael (8).

In a study performed by Burges *et al.* (2) hyperten-

Table 2: Biochemistry data and their statistical analysis of group I and group II, during the following periods (NS = Non significant, a=p<0.05, c=p>0.01, d=p<0.005, e=p<0.001).

		Age (years)	Duration of disease (month)	MBP (mm/Hg)	Crea-tinin (mg/dl)	Protein (gr/day)	ESR (mm/hours)	S. Albu-min (gr/dl)	T. lipid (mg/dl)	Choles-terol (mg/dl)	Leucocyte (mm^3)	Ccr (ml/min/ 1.73 m2)
Group I	Pretreatment	30.0±13.6	16.9±8.2	104.0±21.8	1.2±0.5	5.6±3.3 c	68.6±33.0 a	2.9±0.8 NS	1154±381 NS	303±115 NS	6118±2349 NS	62.4±30.4 NS
	6th month	-	-	-	-	1.4±0.3 c	42.1±24.4 d	3.3±0.5 c	1041±365 NS	252±87 NS	7007±2544 NS	64.7±30.7 b
	12th month	-	-	-	-	0.8±0.3 c	35.5±20.5 d	3.7±0.5 c	918±200 a	238±54 a	7258±1902 NS	78.2±24.1 b
	24th month	-	-	-	-	0.6±0.4 c	29.8±23.0 e	3.8±0.5 e	886±146 b	224±47 d	7361±2445 NS	78.2±24.1 d
	36th month	-	-	-	-	0.1±0.1	26.7±17.1	3.9±0.3	875±726	196±31	6792±2640	90.1±25.3
Group II	Pretreatment	23.1±8.8	16.9±5.9	107.3±17.7	1.4±0.5	5.3±2.6 NS	64.7±35.0 NS	2.6±0.8 NS	1313±532 NS	338±126 NS	9120±4715 NS	54.4±25.9 NS
	6th month	-	-	-	-	3.1±2.1 NS	55.9±25.6 NS	2.8±0.5 NS	1128±484 NS	292±112 NS	7220±2064 NS	67.0±33.1 NS
	12th month	-	-	-	-	3.5±2.1 NS	61.0±25.1 NS	2.8±0.7 NS	1199±469 NS	322±145 NS	7930±2363 NS	48.8±15.1 NS
	24th month	-	-	-	-	3.3±1.9 NS	62.5±36.3 NS	2.9±0.9 NS	1211±655 NS	304±163 NS	8066±1715 NS	44.8±20.8 a
	36th month	-	-	-	-	4.2±1.2	58.7±38.2	2.6±0.5	1210±338	296±81	8057±198	38.0±16.6
Statisti-cal analysis of two groups	Pretreatment	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
	6th month	-	-	-	-	a	NS	b	NS	NS	NS	NS
	12th month	-	-	-	-	a	b	d	NS	NS	NS	a
	24th month	-	-	-	-	d	d	d	NS	NS	NS	d
	36th month	-	-	-	-	e	NS	c	b	d	NS	e

Table 3: Comparison of the data between the patients who have or have not tubulointerstitial changes and vascular involving in two groups (x=p<0.05).

	Patient (%)	Ccr (ml/min)	Proteinuria (g/day)	MBP (mmHg)	Glomerular Sclerosis (%)	Patient (%)	Ccr (ml/min)	Proteinuria (g/day)	MBP (mmHg)
TI Changes (+)	27.2	51.8±16.4	5.0±3.0 x	124.4±11.6	9.5±3.8	80	61.2±33.0	4.0±2.4	105.0±18.4
TI Changes (-)	72.7	61.3±32.4	6.5±4.2	98.7±21.3 x	0	20	81.0±12.7	12.7±11.7	106.5±23.3
Vascular Involving (+)	18.1	58.7±15.9	5.0±4.2	124.9±16.4	14.2±4.1	90	60.0±27.6	5.7±2.1	106.8±18.6
Vascular Involving (-)	81.9	58.5±31.3	6.3±4.0	104.4±21.5	0	10	111	6	93.3

sion was reported in 25-30% of the patients with MCGN. In our study hypertension was found 53.3% of the patients with MCGN. In our study hypertension was found 53.3% in group I and 63.6% in group II on first admission. This high ratio can be explained by the long duration of the disease which was more than 17 months in our patients.

In a study carried out by Schmitt (7), tubulointerstitial changes on renal biopsy, hypertension and early renal failure were reported as poor prognostic criteria. Also, nephrotic syndrome, decreased GFR, hypertension and existence of epithelial crescent were reported as poor prognostic criteria by Levy (9) and Belgiojosa (1).

In group II, hypertension, decreased Ccr, increased serum creatinine levels were observed in 60% nephrotic syndrome in group I, but this ratio was 72% in group II. These results indicate that nephrotic syndrome, decreased renal function, hypertension, tubulointerstitial changes and glomerulosclerosis on renal biopsy are poor prognostic indicators.

In treatment of MCGN, immunosuppressive, cytotoxic and anti-platelet agents are useful to prevent immun complex depositions. Therefore, those drugs are used alone or in combinations (5,10). The effects of different treatment regimens for MCGN are not entirely clarified. Different results may be due to various characteristic of disease and/or patient groups. Spontaneous remission have been reported, but this condition is generally short-term and transient (10).

Of the 26 patients, 15 (57.6%) was in complete remission while in 11 patients (42.4%) disordered renal function continued at the end of the 36 months (3 patients developed ESRD).

In conclusion we can state that in presentation of nephrotic syndrome, decreased Ccr, hypertension, tubulointerstitial changes and glomerulosclerosis on renal biopsy are indicators of poor prognosis and that glucocorticosteroids, cytostatic and anti-thyrombotic agents are strongly influential on the clinical course of the patients with MCGN.

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