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Schistosoma mansoni-induced mesangiocapillary glomerulonephritis: Influence of therapy

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***Schistosoma mansoni*-induced mesangiocapillary glomerulonephritis: Influence of therapy.** *Schistosomiasis mansoni* has been well documented as one of the causes of infectious glomerulopathy, with mesangiocapillary glomerulonephritis being the most frequent lesion observed in this condition. Twenty-one patients with hepatosplenic *schistosomiasis mansoni* and biopsy-documented mesangiocapillary glomerulonephritis (MCGN) were studied and compared with 19 patients with the idiopathic form of MCGN. Nephrotic syndrome was the most frequent clinical presentation in both groups. At the time of diagnosis nine patients with hepatosplenomegaly (4 with associated arterial hypertension) and 12 (8 with arterial hypertension) among the patients with idiopathic MCGN had renal insufficiency. At the end of the follow-up period 16 patients with hepatosplenic schistosomiasis and MCGN (75.2 months) and 15 with the idiopathic form (52.1 months) had renal failure. Also, when compared at 48 months of follow-up, no difference in renal function could be detected in both groups. No benefits related to anti-parasitic treatment in the schistosomiasis group and immunosuppression therapy in either group could be documented. The progression of the renal disease, as assessed by the reciprocal of serum creatinine versus time, and the survival curve, were not different between the two groups. It is concluded that MCGN in patients with the hepatosplenic form of *schistosomiasis mansoni* is a progressive disease not influenced by anti-parasitic or immunosuppressive therapy, and presents a clinical course similar to that of the idiopathic form.

Mesangiocapillary glomerulonephritis is an important cause of nephrotic syndrome and chronic renal failure. Although frequently idiopathic, it is sometimes associated with inheritable, systemic or infectious disease [1–3]. The clinical course of the idiopathic form of mesangiocapillary glomerulonephritis is characterized by a progression toward advanced renal failure without being clearly influenced by immunosuppressive therapy [1, 3]. The clinical course and the influence of cure or control of the underlying disease on the progression of the secondary form this glomerular disease is unknown.

Schistosomiasis mansoni (*S. mansoni*) has been well documented as one of the causes of glomerulopathy [4–10]. Glomerulonephritis has been documented in 15% of the patients with the hepatosplenic form of this chronic parasitic disease [4, 9]. Although other glomerulopathies have been found, mesangiocapillary glomerulonephritis is the most frequent glomerular lesions associated with *S. mansoni* infection [5, 11]. Even though an association between glomerulopathy and schistosomiasis has been recognized for some time, the course of the *schistosomiasis mansoni*-induced mesangiocapillary glomerulonephritis has not been described. The aim of this study was to analyze the clinical course and the influence of the anti-parasitic treatment, alone or in combination with immunosuppressive therapy, in patients with mesangiocapillary glomerulonephritis and the hepatosplenic form of *schistosomiasis mansoni*, with comparisons to the idiopathic form of this glomerulonephritis.

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Methods

All patients with biopsy proven diagnosis of mesangiocapillary glomerulonephritis who were seen in the Renal Service of the Hospital Professor Edgard Santos, Federal University of Bahia were included in the present study. All patients underwent percutaneous renal biopsy as part of the evaluation of renal disease. The specimens were fixed in Bouin's solution, processed by routine techniques, cut in 2 μm thickness and were stained with hematoxilyn and eosin, PAS, PAS-silver methanamine and Heidenhein's stain for connective tissue, and were read by a renal pathologist. The diagnosis of mesangiocapillary glomerulonephritis was made on the basis of well-documented histologic criteria [12]. In brief, there was involvement of both mesangial area and the peripheral capillary walls; most frequently the glomeruli were increased in size, with some accentuation of lobularity. There was mesangial expansion by cellular proliferation and matrix deposition in some or all the glomeruli. Division into lobular and non-lobular forms was not done since a lack of correlation between degree of lobularity and any clinical feature has been shown [3]. For immunofluorescent studies, renal tissues were frozen, cut into 6 μm sections in a cryostat, and stained with fluorescein-conjugated goat antisera to human IgG, IgM, IgA, C_3 and fibrin (Hyland Lab., Costa Mesa, California, USA).

At the time of the initial evaluation a detailed history and physical examination were obtained. Clinical presentation, evidence of recent streptococcal disease or previous episodes suggestive of acute glomerulonephritis, or evidence of systemic or multiple system disease which could be related to nephrotic syndrome were recorded. Laboratory evaluation included stool examination, urinalysis, 24-hour urinary protein excretion, serum levels of urea nitrogen, creatinine, albumin, cholesterol, fasting blood sugar and C_3. Also, evaluation of the presence of hepatitis B virus surface antigen was performed in most patients.

Schistosomiasis mansoni was diagnosed by the demonstration of viable eggs of *S. mansoni* in stools; no quantitative egg counts were performed. All the patients with schistosomiasis had, on physical examination, enlarged and firm liver, with an irregular surface and prominent left lobe. The spleen was also enlarged in 16 patients. Splenectomy had been previously performed in five cases. Idiopathic mesangiocapillary glomerulonephritis was considered in the absence of any disease that could be related to the glomerulopathy.

For the purpose of the present study, nephrotic syndrome was diagnosed by the presence of edema, urinary protein excretion greater than 3.5 g/24 hr, serum albumin levels below 3.0 g/dl with or without high serum cholesterol levels. Renal failure was defined by serum creatinine above 1.5 mg/dl and/or urea nitrogen above 25 mg/dl. End-stage renal failure was defined by serum creatinine above 10.0 mg/dl or by the need of dialysis therapy. Arterial hypertension was defined when blood pressure was over 140/90 mm Hg.

Patients with nephrotic syndrome were treated with immunosuppressive drugs, and with low salt diets, diuretics and anti-hypertensive medication as needed. Prednisone was administered in a dosage of 60 mg/day for four to six weeks, followed by 60 mg every other day for a month and then gradually discontinued. If no response to the steroid had occurred after six weeks of therapy or a steroid dependence was characterized, cyclophosphamide was added in a dosage of 2 to 3 mg/kg for 8 to 12 weeks, given concommitantly with the steroid. Hycanthone, used in a dosage of 2 mg/kg single dose, parenteral or oxamniquine, 15 mg/kg orally single dose, were used to treat the schistosomiasis. Both drugs are anti-schistosomiasis drugs, which have been shown to cure more than 92% of patients [13].

Remission (spontaneous or induced by therapy) was defined by the absence (complete) or reduction (partial) of proteinuria and disappearance of edema. Relapse was defined by the recurrence of proteinuria after the urine had been free of protein for at least four weeks. The clinical response to steroid therapy was designated as follows: steroid responsiveness, defined as a complete remission during steroid therapy and persistence of remission for at least six weeks after therapy; steroid dependence, defined as a complete remission during steroid therapy but recurrence when dosage was reduced or with relapse occurring within the first month after therapy; and steroid resistance, no remission during four to six weeks of daily therapy. The immunosuppressive therapy was well tolerated and in no instance was it necessary to be discontinued. Besides mild signs of hypertisolism related to steroids and mild and transient leukopenia and, in one patient, alopecia, no other complications related to the therapy were documented.

The clinical course of each patient was evaluated by measuring levels of blood pressure (combined with history of anti-hypertensive drug use), serum levels of urea nitrogen, creatinine, albumin and by the correlation between the reciprocal of serum creatinine and time (months). The survival rate was calculated according to Cutler and Ederer [14].

Results

Forty patients were enrolled in the present study. Twenty-one had the hepatosplenic form of *schistosomiasis mansoni* and 19 had no evidence of systemic and/or metabolic disease (Table 1).

Table 1. Mesangiocapillary glomerulonephritis: General data and clinical presentation

	HS/S	Idiopathic
Sex		
Male	15	11
Female	6	8
Total	21	19
Age, mean *yr*	31.4 ± 0.4	31.2 ± 16.8
range *yr*	12 to 66	11 to 68
Length of disease *months*	14.0	11.5
Follow-up *months*	74.2	52.1
Clinical presentation		
Nephrotic syndrome	20	14
Proteinuria	1	4
Acute nephritis	0	1
Total	21	19

Hepatosplenic schistosomiasis patients

Among the 21 patients with *S. mansoni* infection, 15 were male and 6 female, with a mean age of 31.4 years (range 12 to 66 years). Nephrotic syndrome was the most frequent clinical manifestation of MCGN (20 patient); microscopic hematuria was present in all patients. At the time of the diagnosis of nephrotic syndrome, hypertension was documented in eight patients and renal failure was already present in eight patients (4 patients had hypertension and renal failure). Normal serum cholesterol was documented in nine patients. In one patient the manifestation of renal disease was asymptomatic proteinuria, microscopic hematuria and hypertension with normal renal function. The serum levels of C_3 were assessed in 15 patients (Table 2). These were low in three patients, normal in seven and variable in five. No correlation was found between activity of disease and levels of C_3. The hepatitis B virus surface antigen was positive in only one of the 12 patients studied.

The clinical course of these patients is shown in Table 2. At the end of the observation period (mean of 75.2 months), all the patients whose manifestation was nephrotic syndrome continued with proteinuria, which was greater than 3.5 g/24 hr in 13 individuals. There was progression of renal failure in all the patients who already had renal insufficiency at the time of first evaluation, and another seven patients developed renal failure. In nine of these 15 patients the renal failure was advanced, requiring dialysis therapy. Seven patients developed hypertension during observation. Of the fifteen patients with hypertension at the end of the period of observation, twelve developed renal failure.

Two patients were treated with anti-parasitic drugs, 11 with anti-parasitic and immunosuppressive drugs, and four with immunosuppressive drugs alone. All patients were steroid-resistant and in no patient could a therapeutic response to immunosuppressive drugs, to anti-parasitic drugs, or to the combination of immunosuppressive and anti-parasitic drugs, could be documented. There was no apparent influence of therapy on renal function (Table 3).

Table 4 shows the influence of renal insufficiency and/or

Table 2. Hepatosplenic *schistosomiasis mansoni* and mesangiocapillary glomerulonephritis: Clinical and laboratories data

Sex	Age at onset *yr*	Interval from onset *months*	Initial studies BP *mm Hg*	BUN *mg/dl*	Creat *mg/dl*	Albumin *g/dl*	Cholest *mg/dl*	Prot[d]	Treatment[f]	Final studies BP *mm Hg*	BUN *mg/dl*	Creat *mg/dl*	Albumin *g/dl*	Prot[d]	C_3[e]	Follow-up *months*
Nephrotic syndrome																
F	30	4	150/80	33	—	2.9	395	3+	Steroid + Cyc	160/100	69	5.9	3.6	2+	N	184
M	33	12	140/90	13	—	1.8	650	4+	Steroid + Cyc[b]	210/120	106	10.0	3.4	3+	V	156
F	19	20	120/80	13	0.9	1.0	558	4+	Steroid + Cyc[b]	150/110	27	2.1	5.1	Tr	N	151
M	27	60	140/110	37	2.1	2.2	345	4+	Steroid + Cyc	140/90	200	8.0	2.1	1+	L	132
M	32	1	120/80	25	1.1	2.7	146	4+	Steroid + Cyc[b]	120/80	16	0.7	3.8	3+	V	97
M	40	2	130/80	9	1.2	2.9	214	4+	Steroid + Cyc	200/120	13	0.9	5.3	3+	—	92
M	24	9	130/80	19	1.2	2.9	268	3+	Steroid + Cyc[b]	180/110	41	2.3	2.7	4+	V	84
F	22	60	140/90	12	—	1.9	500	4+	Steroid + Cyc	160/100	164	14.5	3.3	4+	N	77
F	66	24	150/90	30	1.3	2.1	214	3+	Steroid + Cyc[b]	130/80	14	1.4	4.3	Tr	N	73
M	42	5	190/120	20	2.0	2.2	330	3+	Steroid + Cyc[b]	170/110	93	11.3	3.2	1+	N	72
M	33	16	220/160	22	1.4	1.8	495	4+	Steroid + Cyc[b]	150/100	146	15.6	1.7	3+	L	66
M	29	7	160/110	27	1.3	1.9	555	3+	Steroid + Cyc[b]	140/100	13	0.8	4.8	2+	V	61
M[c]	25	1	150/90	33	1.7	2.0	231	4+	Steroid + Cyc[b]	140/100	156	10.8	3.2	3+	L	57
M	36	5	130/90	15	1.1	2.8	208	4+	Steroid + Cyc[b]	150/100	102	8.5	2.2	4+	V	52
M	30	20	150/90	21	1.4	2.0	—	3+	Steroid + Cyc[b]	150/100	33	1.8	—	3+	—	34
F	25	6	140/80	26	—	1.6	447	4+	Steroid + Cyc	140/100	97	7.5	3.0	4+	—	31
M	23	1	150/100	42	1.5	1.9	167	4+	Steroid + Cyc[b]	140/100	132	11.0	—	3+	—	30
M	27	3	140/80	19	1.0	2.5	284	3+	—	120/80	11	1.1	4.1	2+	—	21
M	31	12	120/80	44	1.9	1.0	254	4+	—	120/80	28	1.6	3.9	1+	—	13
M	19	9	110/80	25	1.9	2.5		3+	—	110/80	43	1.5	4.0	2+	N	12
Proteinuria																
F	47	[a]	170/100	19	0.9	2.1	425	1+	—	150/110	16	1.1			N	86

[a] Days
[b] Anti-parasitic treatment
[c] HBsAg = positive
[d] Abbreviations are: Tr, trace; 1+, 10–30 mg/dl; 2+, 40–200 mg/dl; 3+, 200–500 mg/dl; 4+, >500 mg/dl.
[e] Abbreviations are: N, normal; V, variable; L, low.
[f] Abbreviation Cyc is cyclophosphamide

Table 3. Hepatosplenic *schistosomiasis mansoni* and mesangiocapillary glomerulonephritis: influence of therapy on renal function

Therapy	No.	Renal function: Normal	Renal insufficiency	End-stage renal disease
Immunosuppressive	4	1	1	2
Anti-parasitic	2	1	0	1
Immunosuppressive/ anti-parasitic	11	2	3	6
No therapy	4	2	2	0
Total	21	6	6	9

Table 4. Mesangiocapillary glomerulonephritis: influence of hypertension and/or renal failure on outcome

	Patients	Renal function: Normal	Renal failure	End-stage
Hypertension				
HS/S	5	2	0	3
Idiopathic	6	1	4	1
Renal failure				
HS/S	4	0	3	1
Idiopathic	1	0	0	1
Both				
HS/S	4	0	0	4
Idiopathic	8	0	4	4
Total	28	3	11	14
None				
HS/S	8	4	3	1
Idiopathic	4	3	0	1

hypertension at the time the patient was initially seen, and the outcome. There was progression or development of renal failure in most of them, particularly among the patients with both conditions at the time of diagnosis of nephrotic syndrome. No correlation was found between levels of C_3 and prognosis, although three patients with persistent hypocomplementemia developed renal failure. Histologically there was no peculiar finding related to this group of patients: the glomeruli were enlarged with some lobular accentuation due to hypercellularity and splitting of the glomerular basement membrane. The hypercellularity included mesangial and endothelial cells and occasionally mononuclear cells. Only a few sclerotic glomeruli were seen on the initial renal biopsy. From immunofluorescent observation granular deposits were seen, consisting predominantely of IgM, IgG, C_3, and, occasionally, fibrin. No relationship between any specific finding and outcome could be documented.

The survival rate is presented in Figure 1: 88% at the end of

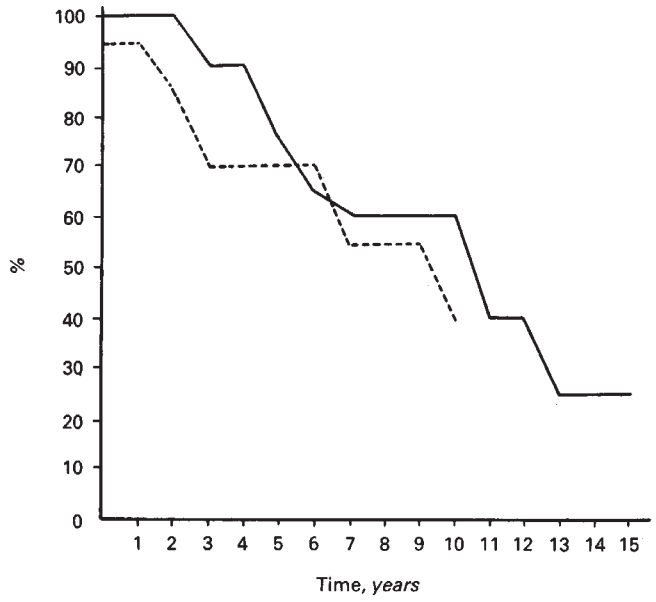

Fig. 1. *Survival rate in patients with mesangiocapillary glomerulonephritis.* Symbols are: (——) hepatosplenic MCGN; (– – – –) idiopathic MCGN.

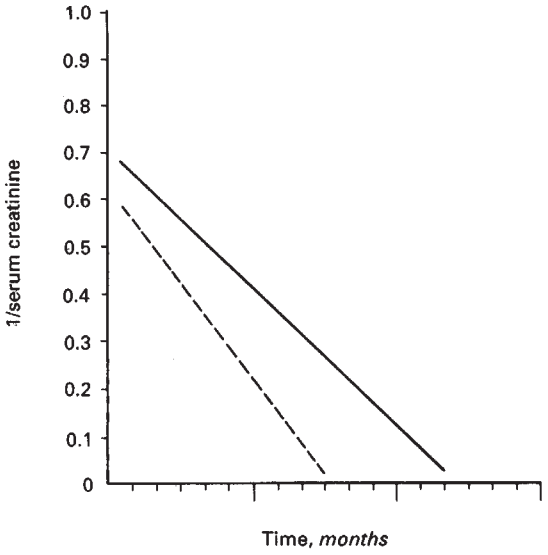

Fig. 2. *Reciprocal of serum creatinine with time in patients with mesangiocapillary glomerulonephritis.* Symbols are: (——) hepatosplenic MCGN, r = 0.8637, y = 0.7289 − 0.116x; and (– – – –) idiopathic MCGN, r = 0.7607, y = 0.6105 − 0.168x.

three years, 76% at the end of five years and 57% at the end of 10 years from the first documentation of proteinuria. The mean interval period between the first documentation of renal failure and the need for dialysis was 51 months (range 10 to 132 months). The correlation between the reciprocal of serum creatinine and time is shown in Figure 2 ($r = 0.86$, $y = 0.73 - 0.01x$).

Idiopathic mesangiocapillary glomerulonephritis

Eleven patients were male and eight were female, with a mean age of 31.2 years (range 11 to 52 years). The clinical manifestation of the glomerulonephritis were (Table 1) nephrotic syndrome in 14 patients (10 already with renal failure, and 11 with arterial hypertension). Four patients presented with asymptomatic proteinuria and normal function (two of them being hypertensive), and one patient presented with nephritic features and normal renal function. Five patients had persistently normal serum levels of C_3, and two had low levels. No correlation was found between activity of disease or presence of HBsAg and complement levels. Hepatitis B virus surface antigen was positive in three of eight nephrotic patients (Table 5). At light microscopic examination the findings were similar to that observed in patients with hepatosplenic schistosomiasis, although, in immunofluorescent studies there was a predominant deposition of IgG, C_3 and IgM.

At the end of the follow-up at 52.1 months (range 10 to 124 months), all patients still had proteinuria, being in nephrotic ranges in 10 and intermittent in one patient. Two patients developed hypertension and three developed renal failure (one patient had transient renal insufficiency at the time of this evaluation). The patients with clinical manifestations other than nephrotic syndrome also presented a progressive course similar to the patients with nephrotic features.

As in the group of patients with *schistosomiasis mansoni*, arterial hypertension and/or renal failure already present at the first evaluation were associated with a progressive course. No relationship was found between presence of HBsAg, levels of C_3 and the presence or absence of lobulation in the glomeruli and clinical course. Regarding the use of immunosuppressive drugs, nine nephrotic patients were treated, and partial remission was observed in one patient. No difference was apparent between the treated and untreated patients. The interval between the first documentation of renal failure and the progression to end-stage renal failure were not different from the *schistosomiasis mansoni* groups ($P < 0.05$ at 42 months). In addition the survival rate (72% at 3 and 5 years and 37% at 10 years, Fig. 1) and the rate of progression of renal failure ($r = 0.76$; $y = 0.61 - 0.01x$) did not differ between these groups (Fig. 2).

Except for the finding of hepatosplenomegaly on the physical examination, the clinical manifestations, course and prognosis as evaluated by the relationship between reciprocal of serum creatinine over time and survival rate, were similar in both groups. In order to rule out the length of follow-up as a selective factor, both group of patients were analyzed at 48 months with regard to renal function. No differences could be documented.

Discussion

The association between glomerulonephritis and *S. mansoni* is well established on the basis of clinical and laboratory studies [4–10, 15–17]. Antigenic material from different morphological stages of *S. mansoni* has been documented in the serum and urine of infected animals and humans [7, 8, 16–18]. In addition, a large molecular weight, negatively-charged proteoglycan, extractable from the gut of the worm, has been identified in the glomeruli of infected humans and animals with portal hypertension [6, 8, 19–23]. Furthermore, glomerular lesions similar to the ones found in humans have been produced in animals infected with *S. mansoni* [7, 24]. Even though the search for

Table 5. Idiopathic mesangiocapillary glomerulonephritis: Clinical and laboratories data

			Initial studies							Final studies						
Sex	Age at onset *yr*	Interval from onset *months*	BP *mm Hg*	BUN *mg/dl*	Creat *mg/dl*	Albumin *g/dl*	Cholest *mg/dl*	Prot[e]	Treatment[d]	BP *mm Hg*	BUN *mg/dl*	Creat *mg/dl*	Albumin *g/dl*	Prot[e]	C_3[f]	Follow-up *months*
Nephrotic syndrome																
M[c]	17	24	140/70		1.5	2.6	172	4+	Steroid + Cyc	120/80	16	1.2	4.0	1+	N	124
F	25	5	180/140	17	1.3	3.0	234	3+	—	120/110	18	1.1	3.6	3+	N	123
F	13	10	150/100	21	2.1	1.7	477	4+	Steroid + Cyc	170/120	67	10.0	2.6	1+		118
M	23	10	140/80	15	1.5	2.2	217	3+	Steroid + Cyc	130/90	188	10.0	2.7	3+		73
M	12	[b]	130/80	18	2.8	1.4	338	4+	Steroid + Cyc	140/100	76	5.6	2.9	4+		57
F[c]	60	2	200/120	28	1.7	3.0	326	3+	—	180/90	43	3.2	4.0	1+	L	48
F	19	24	180/120	26	1.8	2.5	286	3+	—	140/100	44	3.5	3.2	4+	N	46
M	45	4	200/100	9	1.0	2.9		4+	Steroid	160/100	34	1.7		2+		41
F	68	3	210/130	19	1.5	1.9	400	3+	—	200/100	43	4.0	2.4	3+		36
M	37	12	140/100	27	2.2	1.3	201	4+	Steroid + Cyc	150/100	46	1.9	2.7	4+		29
M[c]	39	6	170/110	32	3.8	2.4	400	4+	Steroid + Cyc	180/100	124	10.0	1.4	3+		29
M	28	5	150/100	49	1.8	1.7	374	4+	Steroid + Cyc	160/120	138	10.0		3+	N	18
M	11	5	150/120	20	2.8	1.8	228	3+	Steroid + Cyc	130/90	48	3.0	2.0	4+		17
M	52	6	160/110	34	1.8	1.8	173	4+	—	140/90	149	10.0	2.2	3+		10
Abnormalities of urinalysis																
M[a]	31	9	140/100	13	0.8	4.3	204	1+	—	160/110		14.0	4.8	1+	N	34
F	52	60	150/120	17	1.0	3.3	313	2+	—	180/110	23	2.5	2.6	4+		53
F	21	[b]	180/120	16	1.1	5.4	237	3+	—	140/110	129	15.0	3.8	3+	L	24
F	30	[b]	105/80	18				2+	—	120/80	13	1.0	3.8	3+		73
M	11	12	110/60	14		4.1	220	3+	Steroid + Cyc	110/60	14		3.4			38

[a] Patient with nephritic features
[b] Days
[c] HBsAg positive
[d] Cyc, cyclophosphamide
[e] Proteinuria: 1+, 10–30 mg/dl; 2+, 40–200 mg/dl; 3+, 200–500 mg/dl; 4+, >500/dl.
[f] L, low; N, normal.

deposition of parasitic antigen in the glomeruli of the hepatosplenic *S. mansoni* infected patients was not performed, in this study, there are several points which suggest a specific form of glomerular disease in such cases [5, 6, 10]. All of them came from an area endemic for *S. mansoni*, had documented parasitic infection and exhibited a severe form of this disease. No previous history of nephropathy and no other possible associated condition was documented in any of the cases. Identification of antigen in glomeruli is difficult, not only because it is present in small amounts but also because it could be masked by immunoglobulin and complement [26]. In addition, a gradual decline and disappearance over time of these antigens in the glomeruli of chronically infected animals and humans have been shown [8, 25].

In the patients studied, except for the findings of hepatosplenomegaly on physical examination directly related to the *S. mansoni*, no other difference, either clinical or histological could be found between the groups. Nephrotic syndrome was the most frequent clinical presentation of the mesangiocapillary glomerulonephritis in both groups of patients. Although renal failure present at time of the first evaluation was more common among the patients with the idiopathic form of glomerulonephritis, it was not considered to be a peculiar finding of these patients. The clinical course of the disease was also similar and progressive in both groups. Such progression was more rapid among the patients who presented with renal insufficiency and/or hypertension. The renal failure suggests a more advanced glomerular lesion, and the aggravation role hypertension in the course of glomerular disease is well known.

The rate of progression of the renal failure, as assessed by the relationship between the reciprocal of serum creatinine and time, was also similar in both groups. Although not all patients with renal failure presented a linear decline of renal function, it seems to be a reliable method for the evaluation of progression of renal failure. In our series, at time of the final evaluation 70% of the patients in each group had developed renal failure. Also, no difference in relation to renal function could be documented when the patients were evaluated and compared at 48 months of follow-up. Considering the survival rate, even though it seemed to be higher among the patients with *schistosomiasis mansoni* at three years, it was not statistically different, and tended to be very similar at five and 10 years, and not different from the survival of nephrotic patients as documented by others [1–3, 27–29].

The importance of serum levels of C_3 in the clinical detection of glomerulopathy in patients with hepatosplenic schistosomiasis has been reported [30, 31]. In the present study, however, we could not document any relationship between the levels of complement and the clinical course or prognosis of the disease. The three patients with persistent hypocomplementemia developed end-stage renal failure during the follow-up period, but the number of patients with this finding is small and does not permit any conclusion. The lack of correlation between complement levels and course and prognosis of the mesangiocapillary glomerulonephritis was also observed in patients with the idiopathic form, as has already been reported [3]. Also there was a lack of a characteristic finding on the histological light microscopy studies of the renal biopsies of the *S. mansoni* group of patients.

As in the group of patients with the idiopathic form of

mesangiocapillary glomerulonephritis, the use of immunosuppressive drugs did not influence the course of the disease in patients with *schistosomiasis mansoni*. Persistent disappearance of proteinuria or influence in the outcome of renal function, as reported in other forms of glomerular disease, could not be documented. Except for uncontrolled studies [32, 33], unresponsiveness to immunosuppressive therapy has been found in most studies of patients with mesangiocapillary glomerulonephritis [1, 3]. Also, no benefit could be documented by using anti-parasitic drugs, alone or in association with immunosuppressive therapy, despite the cure of the parasitic infection. Additionally, no detrimental effect related to the parasitic therapy was apparent [34]. Experimental studies have shown the importance of the length of infection at the time of anti-parasitic treatment on the renal disease. Sadum et al [35] while studying the influence of anti-parasitic therapy on the evolution of schistosomiasis in chimpanzees, documented that treatment early in course of the infection prevented or halted the renal lesions, as compared with untreated or late-treated animals. Valadares and Pereira [36] also documented the disappearance of urinalysis abnormalities only in mice treated in the first week after *S. mansoni* infection.

Our data suggest that mesangiocapillary glomerulonephritis in patients with hepatosplenic form of *S. mansoni* infection is a progressive disease, and shows a clinical course similar to that of the idiopathic form. Once the glomerulopathy is already established and clinically manifested, it seems to progress to an advanced stage, where the hemodynamic adaptations that follow reduction of functional renal mass are already present [37] independently of the presence or absence of the parasite. This emphasizes the importance of early diagnosis and therapy of the *S. mansoni* infection.

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