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Nephropathy in Asymptomatic Patients with Active Schistosoma mansoni Infection

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In this study 240 patients with active *Schistosoma mansoni* infection with no symptoms suggestive of glomerular disease were subjected to investigation. All were evaluated clinically and their urine was examined for proteinuria.

Out of the 240 patients 48 (20%) had proteinuria as detected by the dipstick test. All these patients were found to be free of any secondary cause other than schistosomiasis which could explain their proteinuria. Out of these 48 patients, 15 agreed to be subjected to kidney biopsy. When examined by light microscopy and immunofluorescent microscopy, kidney biopsies showed positive findings in 8 cases. These were mainly focal mesangial proliferation and immunofluorescent deposits which were mainly IgM and C_3. We have concluded that early kidney lesions could be detected in 20% of this particular group of patients.

Introduction

Schistosomiasis is a chronic helminthic disease of man and animals. It is endemic in vast areas of South America, Africa and Asia. Estimates by WHO give figures of 200 million infected people.

The adult worm and eggs were found to be highly antigenic to man and experimental animals [1, 2, 3]. Since schistosomal infection if not treated may persist for 10–12 years, chronic antigenaemia is expected to be a feature of this disease. Diseases which chronically stimulate the host as hepatitis B virus infection have been shown to induce glomerulonephritis [4], thus similar renal lesions are expected to develop with schistosomiasis. Andrade et al. [5] reported that 12–15% of patients with hepatosplenic schistosomiasis have glomerulonephritis.

Portal hypertension with portosystemic collaterals were reported to play a role in the pathogenesis of the disease [6].

Information regarding the prevalence of nephropathy among patients with active *Schistosoma mansoni* infection in our community is still lacking. The objective of this work was to study the glomerulopathy in our patients with active *Schistosoma mansoni* infection especially those who were asymptomatic.

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Materials and methods

A total of 240 patients with active *Schistosoma mansoni* infection presenting at the outpatient clinic of the Department of Internal Medicine asking for treatment of their disease were admitted to the study. All were asymptomatic regarding their kidney and urinary system, i.e. no puffiness, oedema, dysuria, oliguria, turbidity of urine or loin pains.

All patients were evaluated clinically with special stress on the presence of hepatosplenomegaly and proteinuria. Proteinuria was tested by using dipsticks and patient's fresh urine.

Those showing proteinuria were admitted to the Nephrology Department of the Urology and Nephrology Center where they were subjected to the following examinations:

1. Rectal mucosal biopsy, to confirm the active *Schistosoma mansoni* infection by finding the living ova with their characteristic lateral spikes.

2. Clinical evaluation, to exclude the different aetiologic causes which can explain the presence of proteinuria such as recurrent throat infection, diabetes, systemic lupus erythematosus and drug-induced nephropathy.

3. Laboratory investigations, to evaluate the renal involvement by determination of serum creatinine, creatinine clearance and 24-hour urinary protein excretion. In addition, investigations were done to exclude secondary causes of glomerulonephritis such as LE cells, anti-DNA to exclude SLE and postprandial blood sugar to exclude diabetic nephropathy.

4. Kidney biopsy. Under fluoroscopic guidance and using a true-cut biopsy needle and after injection of contrast media to visualize the pelvi-calyceal system a percutaneous needle biopsy was performed. Two cores of kidney tissue were obtained from the lower pole of the right kidney.

(a) The first core was fixed in 10% formalin and paraffin sections were obtained and stained with haematoxylin and eosin, mathon trichrome, PAS and congored stains. Sections were examined by light microscopy.

(b) The second core was immediately frozen and stored at -70 °C. From this core, frozen sections were prepared and examined by direct immunofluorescence for different immunoglobulins and complement component deposits. Sections were stained with fluorescein-labelled antihuman IgG, IgM, IgA, C_3, C_4, C_{1q} and fibrinogen.

Results

Two hundred and forty patients (166 males and 74 females) with active *Schistosoma mansoni* infection were examined. Of the patients 85% were 15–40 years old, 6.6% were below 15 and 8.4% were above 40 years. Infection occurred in 33.3% once, in 59.5% twice, in 5.4% three times and in 1.6% more than three times. Of the patients subjected to this study 17% showed hepatosplenic and 83% hepatointestinal schistosomiasis. Out of the 240 patients examined 48 (20%) had

Table 1

Histopathological and immunofluorescent findings in 15 patients with active *Schistosoma mansoni* infections

Case No.	Light microscopy	Immunofluorescent deposits
1	N. A. D.	C_3
2	N. A. D.	—
3	Mild focal mesangial proliferation	IgM, IgG, C_3
4	N. A. D.	—
5	N. A. D.	—
6	Mild focal and mesangial proliferation	IgM, C_3
7	Mild focal mesangial proliferation	IgM, C_3
8	N. A. D.	—
9	N. A. D.	—
10	N. A. D.	—
11	Focal mesangial proliferation, focal tubular atrophy, focal fibrosis	IgM, C_3
12	Focal mesangial proliferation	C_3
13	N. A. D.	C_3
14	Focal mesangial proliferation	IgM, C_3
15	N. A. D.	—

N. A. D. = no abnormality detected (by light microscopy).

proteinuria; 38 were males and 10 were females, 85.3% of them were 15–40 years old, 6.3% were under 15 and 8.4 were over 42 years. Of these 35.4% were infected once, 54.1% twice and 10.4% three times or more. Out of the 48 patients with proteinuria, 38 were hepatointestinal and 10 were hepatosplenic; 15 gave consent to be biopsied. Table 1 shows the findings of kidney biopsies examined by light and immunofluorescent microscopy. Light microscopic changes were discovered in 6 cases, these were mainly mild, focal mesangial proliferative (Fig. 1). In all of these 6 cases and in 2 cases with no abnormality detected by light microscopy there were immunofluorescent granular deposits which were mainly C_3 and IgM in nature, mesangial and capillary wall in distribution (Fig. 2).

We could not find any relationship between the form of schistosomal disease and the presence or absence of light and/or immunofluorescent microscopic changes (Table 2).

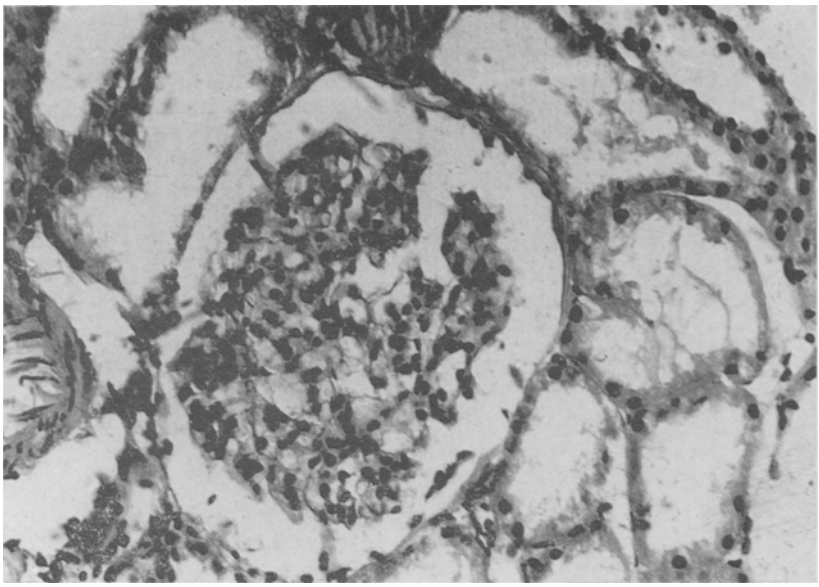

Fig. 1. Kidney biopsy: mild mesangial proliferation (HE, × 400)

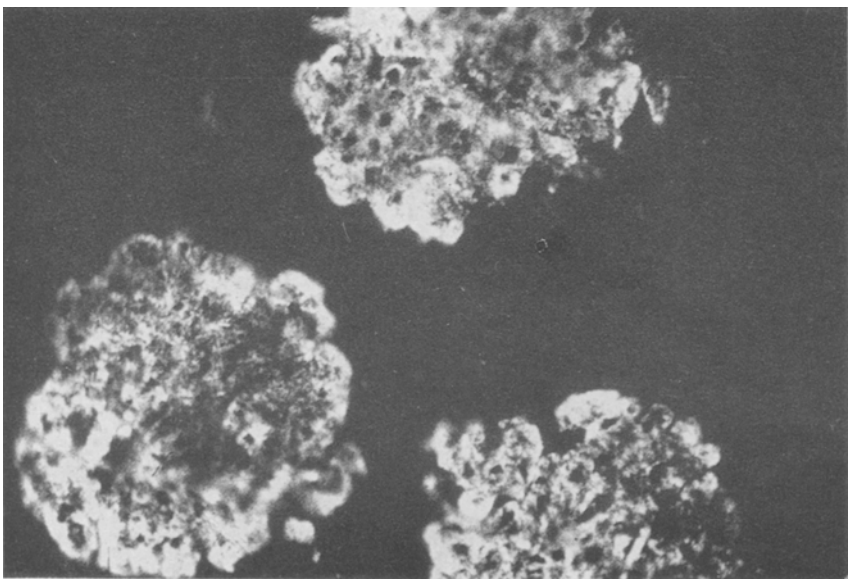

Fig. 2. Kidney biopsy: diffuse capillary wall and mesangial deposits of IgM. (Direct immunofluorescence, × 250)

Table 2

Relationship between the form of schistosomal disease and the presence or absence of glomerular changes

	Presence	Absence	Total*
Hepatointestinal	4	3	7
Hepatosplenic	4	4	8
Total*	8	7	15

* Number of cases

Discussion

The first reference to urine abnormalities in schistosomiasis caused by *Schistosoma mansoni* was made by Lopez in 1964 [7]. He analyzed 105 patients suffering from the hepatosplenic form and discovered in 26.7% of them urinary abnormalities (proteinuria and leucocyturia) of clinical importance. In contrast, only 3.8% of 105 patients suffering from hepatointestinal form showed urinary abnormalities. Subsequently, in a light microscopic study of 38 kidney biopsies obtained from patients with hepatosplenic schistosomiasis with or without clinical evidence of renal disease, Brito [8] found in 76.4% glomerular alterations. Furthermore, Rocha et al. [9] found in selected cases of hepatosplenic schistosomiasis, seen in a general hospital or examined at necropsy, overt renal involvement in 12 to 15%, whereas the overall incidence of glomerulonephritis was 5.6%.

Recently, Bena et al. [10] detected proteinuria in 24.7% of 89 individuals with hepatosplenic schistosomiasis and in only 4.6% of 86 subjects with mild hepatointestinal schistosomiasis.

Since the real prevalence of schistosomal renal involvement in endemic areas is not known [11], and most of the reported studies describe findings in South America, especially Brazil, the objective of this work was to report the findings in Egypt, another endemic area. A special group of patients was selected to study the disease process: these are the patients with active *Schistosoma mansoni* infection with no renal symptoms. We considered this group important, since if the disease does exist it will be in the very early phase. Out of the 245 patients examined, 48 (20%) showed proteinuria by the dipstick test. It was observed that 79% of them were in the hepatointestinal phase of schistosomiasis, suggesting that glomerulopathy may occur in the absence of portal hypertension and portosystemic collaterals. This could be explained by the possibility of high load of infection and consequently high antigen load causing spillover of the hepatic filter and reaching the renal glomeruli. Another possibility is that the presence of adult worms in the circulation may excite an autoimmune mechanism causing renal disease [12].

Light microscopic examination of renal biopsy specimens from 15 cases showed changes in 6. In two cases there was no change, yet there were immunofluorescent deposits indicating the presence of lesions which may be detected if kidney biopsies were examined by electron microscopy. The light microscopic findings were mesangioproliferative in nature and focal in distribution. C_3 deposits were found in all of the positive cases, IgM in 5 and IgG in only one case.

Andrade and Queiroz [13] and Brito et al. [14] reported that the mesangial area of the glomerulus is the main site of lesions of schistosomal nephropathy. In the least advanced cases there was mesangial expansion due to the presence of amorphous and fibrillar PAS-positive material, as well as mesangial cellular hypertrophy and hyperplasia. Electron microscopy disclosed electron-dense deposits and laminar bodies in mesangial areas [14]. It is also in such areas that the main deposition of IgG, IgM, IgA, IgE and C_3 occurs as demonstrated by immunofluorescence [15].

From these results we have concluded that patients with active *Schistosoma mansoni* infection may have kidney lesions even when they are symptom-free. These lesions could be detected by light microscopy and/or immunofluorescent microscopy. In some cases more sensitive techniques, such as electron microscopy, are needed to detect these lesions. The lesions in these patients in the early phase are mainly mesangial and the deposits are mainly IgM and C_3.

In our patients no correlation was found between renal lesions and the stage of the schistosomal disease.

Finally, screening of the susceptible population for schistosomiasis and for proteinuria is mandatory since early diagnosis and eradication of the disease may abort the renal affection in its early phase.

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