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Clinical and Morphological Changes in non Obstructive Renal Tuberculosis

Rana Gopal SINGH, USHA, Indrajeet Singh GAMBHIR and Jayant MATHUR

Department of Nephrology, Pathology, Institute of Medical Sciences, Banaras Hindu University, Varanasi-221 005, INDIA

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ABSTRACT

Renal histopathology in non-obstructive stage of urinary tuberculosis revealed seven types of lesion viz; a) nil lesion without nephrotic syndrome (35%); b) minimal change glomerulonephritis (15%); c) focal global sclerosis (5%); d) focal segmental proliferative glomerulonephritis (5%); e) chronic pyelonephritis (15%); f) amyloidosis (20%) and g) focal segmental glomerulosclerosis (5%).

Patients having nil lesion without nephrotic syndrome were young, presented with hematuria (57.14%) and positive IVP abnormalities (71.42%) with nil to mild proteinuria. Patients with sclerosing and proliferative lesions mainly presented with hematuria and 2/3 had IVP abnormalities. Amyloidosis patients had generalized swelling all over body with blood pressure towards lower side of normal, marked proteinuria and hypoalbuminemia, 50% of them had long standing pulmonary tuberculosis with normal IVP findings.

In last 100 years since Koch's discovery of tubercle bacillus; a lot of challenging work has been done to overcome this dreaded disease. Especially in last 2½ decades the advent of antitubercular chemotherapy has changed the whole scene. Inflammatory and obstructive stage of genito urinary turberculosis have received much attention in preantibiotic era. There is little information in the literature particularly from India regarding non-obstructive genito-urinary tuberculosis[3,4]. Further more antemortem studies of renal morphology are very sparse in literature, since renal biopsy has not been a universal procedure in genito-urinary tuberculosis. This study has been undertaken to document changes in renal morphology in the early non-obstructive stage of renal tuberculosis and to study its correlation with clinical presentation and radiological investigations for a better understanding of the early stage of diseases so as to prevent morbidity.

MATERIAL AND METHOD

The present study comprised of the cases satisfying the following criteria of genito-urinary tuberculosis.

1. Demonstration of presence of Acid-fast bacilli in urine in any one of the four consecutive morning samples of urine, which was grown in Lowenstein-Jensen media.
2. Intravenous pyelogram should not have any features of obstruction in urinary tract.

Altogether 20 patients fulfilled these criteria. They were subjected to detailed history and clinical examination. Investigations like urinalysis, blood urea, serum creatinine and electrolytes, total protein and A:G ratio, 24 hr urinary protein and urine culture for AFB were undertaken. Radiological investigations like I.V.P., X-ray chest and bones in relevent cases were un-

Mailing Address: Dr. R.G. Singh, MD., DM., MNAMS., Head, Division of Nephrology, L-15, Hydrabad Colony, Banaras Hindu University, Varanasi-221 005, INDIA

Table 1. Clinico-histopathological correlation of the cases

Histological types	NO.	%	Age Groups			Proteinuria		Hematuria		Renal Insuffi.	
			<20	21—40	41.60	<3.5gm (N.N.S.)	>3.5gm (N.S.)	No.of cases	%	No.of cases	%
Nil lesion without nephrotic syndrome.	7	35.0	14.28%	85.71%	—	100%	—	4	57.14	—	—
Minimal change glomerulonephritis.	3	15.0	100%	—	—	—	100%	1	33.33	1	33.33
Focal segmental proliferative glomerulonephritis.	1	5.0	—	100%	—	100%	—	1	100.00	—	—
Focal global sclerosis.	1	5.0	100%	—	—	100%	—	1	100.00	—	—
Focal segmental glomerulosclerosis.	1	5.0	—	100%	—	100%	—	1	100.00	—	—
Chronic pyelonephritis	3	15.0	—	—	100%	33.33%	66.66%	2	100.00	1	33.33
Amyloidosis	4	20.0	25%	50%	25%	—	100%	—	—	3	75.00

N.S. = Nephrotic Syndrome
N.N.S. = Non Nephrotic Syndrome

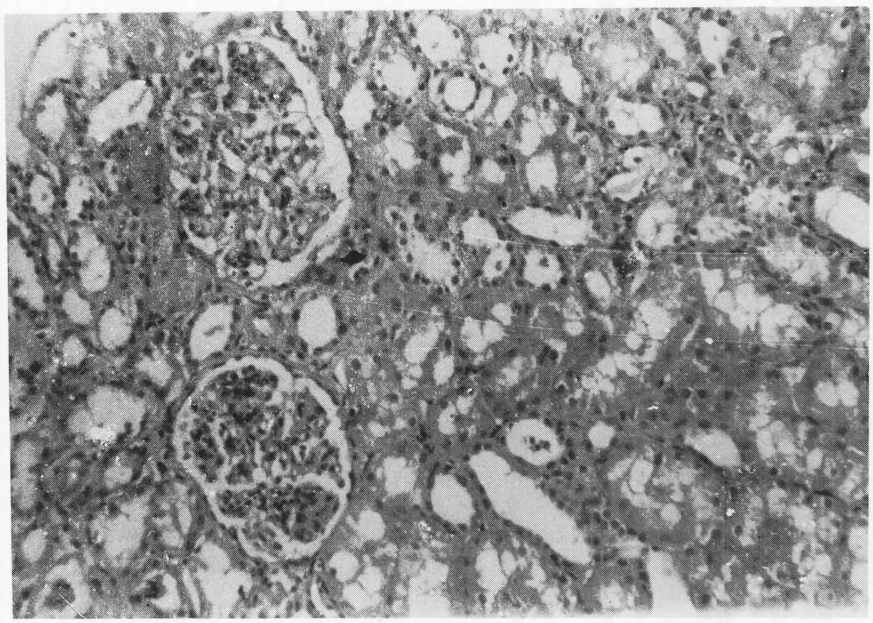

Fig. 1. Shows focal segmental proliferative changes in the glomerulus, surrounding tubules are showing Vacuolar degeneration. (H & E × 125).

dertaken.

All the 20 patients were subjected to renal biopsy by percutaneous route using Vim-Silverman's needle with Franklin's modification. Renal tissue thus obtained was fixed in 10% formalin and routine paraffin blocks were prepared. 2 μ thick sections were cut and stained with haematoxylins-eosin, PAS, PASM and congored in all the cases.

OBSERVATION

The lesions were classified as per Turner's 1978 classification. The nil lesion without nephrotic syndrome was the commonest lesion

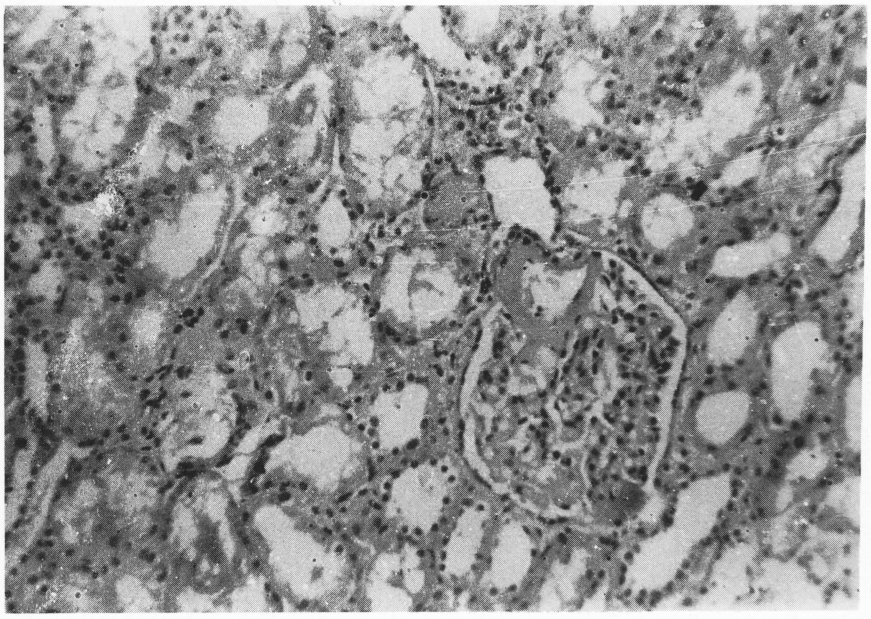

Fig. 2. Shows amyloid deposition in the glomerular capilary loop and mesangium (H & E × 125).

Table 2. Correlation of histopathological varieties with radiological findings

Histopathological varieties	No.of cases	Ponsitive IVP findings	%	Positive tubercular X-ray chest findings	%	Positive tub. osteoarticular findings	%
Nil lesion without nephrotic syndrome.	7	5	71.42	—	—	—	—
Minimal change glomerulonephritis.	3	—	—	—	—	1	33.33
Focal global sclerosis.	1	1	100.00	—	—	—	—
Focal segmental proliferative glomerulonephritis.	1	—	—	—	—	—	—
Focal segmental glomerulosclerosis.	1	1	100.00	—	—	—	—
Chronic pyelonephritis	3	2	66.66	2	66.66	—	—
Amyloidosis	4	—	—	2	50.00	—	—

(35%) followed by Amyloidosis in 20%. The minimal change GN is nephrotic state and evidence of chronic pyelonephritis was noticed in 3 (15%) patients each whereas one patient each had focal global sclerosis, focal segmental proliferative and focal segmental glomerulosclerosis (Table 1).

Patients of 'nil' lesion without nephrotic state mainly came in their third and fourth decade of their lives with haematuria in 4 cases. The minimal change with nephrotic syndrome had evidence of haematuria and renal insufficiency in one case each.

The patient with focal segmental proliferative GN (Fig. 1) was 27 years old male with haematuria, hypertension and mild proteinuria, whereas the patient with segmental glomerulosclerosis had right non excretory kidney where

angiogram showed evidence of right renal artery stenosis.

One patient of chr. pyelonephritis came in the stage of chronic renal failure. Renal amyloidosis (Fig. 2) formed a predominent group in renal tuberculosis. The eldest person was 60 years old male with long standing pulmonary tuberculosis. All came in nephrotic state with hypoproteinemia and hyperlipidemia. All had blood pressure on the lower side of the normal and two patients had renal insufficiency.

Thus seeing the overall picture, few evident things are that nephrotic range proteinuria without hematuria is suggestive of either amyloidosis or minimal lesion glomerulonephritis. Long standing tuberculosis of lungs or other organs in elderly with hypotension is probably due to amyloidosis. However in young patients differentiation is not possible.

Non nephrotic range proteinuria without hematuria is more suggestive of nil lesion or focal glomerular lesion in patients under 40 years and of chronic pyelonephritis in patients over 40 years of age group.

A correlation of histopathological lesion with renal insufficiency reveals that 50% cases of amyloidosis and 33% cases of minimal lesions were having renal insufficiency. Renal damage was also seen in a patient of chronic pyelonephritis (33%). No azotemic features were seen in patients of non obstructive renal tuberculosis with nil lesions or focal glomerular lesions. Table 2 depicts correlation of histopathological varieties with radiological findings. In general 45% patients showed positive I.V.P. evidence of genitourinary tuberculosis. Majority of patients (71.9%) with nil lesion without nephrotic syndrome had I.V.P. change suggestive of primary disease. 2/3rd patients of chronic pyelonephritis also had positive I.V.P. changes. Whereas none of the patients with amyloidosis had positive I.V.P. findings. 50% of cases of amyloidosis and 66.6% of cases with chronic pyelonephritis had Koch's lung.

DISCUSSION

Overall nil lesion without nephrotic range proteinuria dominated the series with an incidence of 35%. The only abnormality was observed in proximal tubules which showed tubular necrosis filled with granular and hyaline cast in their lumen. 50% patients presented with hematuria and 71.42% had IVP abnormalities.

Diffuse amyloid involvement was present in 20% cases and all had nephrotic presentation and even distribution was seen in minimal change glomerulonephritis and chronic pyelonephritis (15%) each. Among the sclerotic lesions, focal global and focal segmental involvement was seen in only one case each. Focal proliferative change was observed in another 5% case and hematuria was a universal feature in all these cases of focal glomerular involvement. Unfortunately histological observation in renal tuberculosis has been only limited to either autopsy study or as morbid anatomy on nephrectomised kidney. In all these conditions, obstructive varieties have always dominated, either due to caseation, abscess formation, ulceration or ureteritis. Hamburger et al[1] has described about the histopathological genesis of tuberculous granulation tissue in true initial stage where bacteria are only localized to cortical area, hence they may not produce any gross histological abnormality. In our 35% cases who presented as nil lesion and non-nephrotic proteinuria, there may be a strong possibility that patients might be passing through such a stage of bacteremia when we isolated acid-fast bacilli from the urine. Out of these 57.14% cases had hematuria which is not possible until unless a breech of discontinuity has occured in glomerular basement membrance or in adjacent tubular basement membrance. This concept is supported by our observation that in majority of the patients we have observed proximal tubular necrosis and this explains the cause of hematuria and radiological abnormalities.

The next incidence in the morbidity was diffuse amyloid deposits observed in 20% cases, none of these patients had hematuria but 50% cases had evidence of renal insufficiency with massive proteinuria (>3.5 g in 24 hr) in all cases (100%). We have observed that 75% of such patients were young adults and only one belonged to sixth decade. This is a little unusual observation as people initially believed that it is chronic pulmonary tuberculosis which is responsible for secondary amyloid deposit in kidney, since we have not explored the possibility of primary versus secondary amyloidosis we cannot be so sure that the amyloid deposit was

secondary to tuberculosis or primary idiopathic variety. We isolated A.F.B. in all these four patients which dectates that active bacteremia was persisting in these patients. All patients showed amyloid deposition in their rectal biopsies as well, henceforth we presume that active bacilluria and secondary amyloid deposit can co-exist in non-obstructive renal tuberculosis.

As an evidence of primary glomerular involvement, minimal change nephrotic syndrome was observed in 15% cases in second decade of life with a nephrotic range proteinuria and 33.66% hematuria. Witting and Goldman[5] in 1970 have also described the association of minimal change nephrotic syndrome following immunosuppressive therapy in renal tuberculosis patients. As such hematuria is an infrequent observation in idiopathic minimal change nephrotic syndrome whereas we have observed that one out of three patients had active hematuria. This finding supports that tuberculosis in some way produce minimal type of glomerular damage either in endothelial slit pore or in mesangial matrix which can give a chance to the R.B.C. to escape in the urinary space. In the absence of electron microscopic studies, above observations are difficult to prove but they favour a possibility of some sort of immune mediated glomerular injury which has resulted in nephrotic range proteinuria and hematuria.

In 15% cases, all belonging to fifth and sixth decades of life presented with histological and radiological feature of chronic pyelonephritis. This has been a classical observation that tuberculosis ultimately produces papillary ulceration and interstitial involvement[1]. In two of these cases focal global sclerosis was also present.

Three patients in this series had evidence of focal and segmental sclerosis and proliferative changes in the mesangium, all these patients had active hematuria. In the absence of any evidence of destructive or ulcerative lesion there has to be some form of glomerular injury which was obvious by our observations since there is a strong lacune of knowledge in this subject and our sample was too small hence, we cannot conclude that all the three type of lesions were an association or cause of direct tubercular involvement.

So in nut-shell the various non-obstructive genitourinary complications in relation to various nephrological syndromes in our study were as follows — asymptomatic urinary abnormalites e.g. hematuria (50%), albuminuria (35%) was the main mode of presentation. 35% patients presented with nephrotic syndrome out of which 20% turned out to be having amyloidosis. 15% each had hypertension and urinary tract infection. While CRF and ARF was observed in only one case each, thus proving that the CRF and ARF are rare manifestations of genitourinary tuberculosis. By our criteria of selection of cases, we have excluded all the patients having associated stone disease, and obstructive uropathy which are usually known late complications of urogenital tuberculosis.

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