

Renal Lesions and Other Major Findings in Necropsies of 133 Patients with Leprosy¹

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There are many recent biopsy studies of kidney lesions in leprosy, but most published descriptions of renal disease in post-mortem material in leprosy are over a decade old (⁸). It was therefore decided to examine the kidneys from a large number of necropsies on leprosy patients and to interpret the findings in light of the recent knowledge gained from biopsy studies. As our study progressed, it became evident that renal disease was an important cause of death in these patients, but that the renal involvement was often secondary to non-leprosy infectious disease in other organs. The scope of the study was therefore widened to include infections and other causes of death in these patients.

In this report the renal lesions found in 133 leprosy patients are presented against a background of disease in other organs.

MATERIALS AND METHODS

During the period 1965–1984, 145 necropsies were performed on patients with leprosy in the Pathology Department of the Christian Medical College Hospital, Vellore, India. Twelve cases were unsuitable for study because of extensive autolysis. Histopathological slides, paraffin blocks, Formalin-fixed organ slices, and clinical case records of the remaining 133 patients comprised the materials for our study. Necropsy findings on 37 patients studied before 1965 and reported earlier (¹) were not included.

Kidney sections stained with hematoxylin and eosin, periodic acid-Schiff, Martius Scarlet Blue for fibrin, and Thioflavin T and Congo red stains for amyloid (¹) were examined, and the lesions classified according

to standard light microscopic criteria (^{12, 24}). Small areas of medullary interstitial sclerosis, nonspecific subcapsular scarring, and focal tubular or papillary calcification were ignored. The gross and microscopic findings in other organs were abstracted from the necropsy records. Infections were diagnosed histologically. Microbial cultures either had not been done or their results were unavailable in most cases.

Since many of the cases had originally been classified before the introduction of the Ridley and Jopling grouping (²¹) and since it was not possible to reclassify these patients, the older classification of leprosy was used (⁷).

Analysis of the data was by means of Chi-square tests.

RESULTS

The 133 patients studied were in the age range of 17–82 years (mean 46, standard deviation ± 13 years). Only 17 were females. Twenty-two patients had borderline leprosy, 9 tuberculoid leprosy and the rest lepromatous leprosy. The recorded duration of the disease after diagnosis was from 1–55 years (mean 15, standard deviation ± 10.5 years). Forty-six patients had recent erythema nodosum leprosum (ENL) reactions, and trophic ulcers were seen in 75 patients.

All patients had been treated with dapsone for varying lengths of time, and 12 patients were given clofazimine. ENL had been treated with potassium antimony tartrate intravenously or with chloroquine. Corticosteroids were used in 9 patients.

Renal lesions. Renal lesions were an important factor contributing to the death of 50 patients whose findings are summarized in Table 1.

Glomerulonephritis was diagnosed in 16 patients who had proteinuria and/or renal failure. The glomerulonephritis was of different histological types, and in four cases was probably secondary to infective endo-

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TABLE 1. Major renal lesions in 50 patients with leprosy.

Case no.	Age and sex	Type of leprosy ^a	ENL ^b	Trophic ulcers	Major renal lesions	Other most relevant lesion
1	37 M	L	+ ^c	+	Diffuse endocapillary proliferative GN ^e	None
2	60 M	L	- ^d	+	Diffuse endocapillary proliferative GN	Bronchopneumonia
3	35 M	L	+	-	Diffuse endocapillary proliferative GN	None
4	65 M	L	-	+	Diffuse mesangial proliferative GN	None
5	38 M	L	-	-	Diffuse extracapillary GN	Amebiasis, colon and liver
6	40 M	L	+	-	Diffuse extracapillary GN	None
7	55 M	L	+	+	Diffuse extracapillary GN	None
8	69 M	L	-	+	Diffuse mesangiocapillary GN	None
9	40 M	L	-	-	Diffuse mesangiocapillary GN	None
10	27 M	L	-	-	Diffuse mesangiocapillary GN	None
11	62 M	T	-	+	Focal proliferative GN	Lung abscess
12	33 M	L	+	+	Diffuse endocapillary proliferative GN	Infective endocarditis
13	24 M	L	-	+	Diffuse endocapillary proliferative GN	Infective endocarditis
14	51 F	L	-	+	Focal proliferative GN and abscesses	Infective endocarditis
15	50 M	B	-	+	Focal proliferative GN and abscesses	Infective endocarditis
16	52 M	L	+	-	Focal proliferative GN and abscesses	Bronchopneumonia with abscesses
17	27 M	B	-	+	Abscesses	Infective endocarditis
18	46 M	B	-	+	Abscesses	Infective endocarditis
19	43 M	B	-	+	Abscesses	Infective endocarditis
20	27 M	L	-	+	Abscesses	Meningitis
21	45 M	T	-	+	Abscesses	Bronchopneumonia with abscesses
22	27 F	B	-	+	Abscesses	Lobar pneumonia with abscesses
23	55 M	L	-	+	Abscesses	Bronchopneumonia with abscesses
24	48 M	B	+	+	Abscesses	Bronchopneumonia with abscesses
25	46 M	B	+	+	Abscesses	Lung abscess
26	55 M	L	+	+	Fibrin deposits	Bronchopneumonia
27	48 F	L	-	+	Fibrin deposits and ATN ^f	Bronchopneumonia
28	66 M	L	-	+	Fibrin deposits and ATN	Brain abscesses
29	51 M	B	+	-	Fibrin deposits and ATN	Empyema
30	38 M	L	-	+	Fibrin deposits	Gangrene, leg
31	55 F	T	-	+	Fibrin deposits and ATN	Infected ovarian cyst
32	50 M	B	+	+	Fibrin deposits and ATN	Acute enterocolitis
33	53 M	L	-	-	Fibrin deposits and ATN	Infective endocarditis
34	40 F	L	-	+	Fibrin deposits and ATN	Bronchopneumonia
35	45 M	L	-	-	Fibrin deposits and ATN	Poisoning
36	30 M	L	-	+	Amyloidosis	Lung abscess
37	40 M	L	+	+	Amyloidosis	None
38	22 M	L	+	+	Amyloidosis	None
39	35 M	L	+	+	Amyloidosis	None
40	47 M	L	-	-	Amyloidosis	Disseminated tuberculosis
41	35 M	L	+	+	Amyloidosis	None
42	38 M	L	-	+	Amyloidosis	Pulmonary tuberculosis
43	40 M	L	+	+	Amyloidosis	Tuberculous lymphadenitis
44	49 M	L	-	+	Amyloidosis	Pulmonary tuberculosis
45	32 M	B	-	-	Amyloidosis	Disseminated tuberculosis
46	36 M	T	-	-	Chronic pyelonephritis	Lobar pneumonia
47	65 M	L	-	+	Chronic pyelonephritis	Bronchopneumonia
48	73 M	L	-	+	Chronic pyelonephritis	Elephantiasis, leg
49	42 M	L	+	+	Chronic pyelonephritis	Hodgkin's disease
50	52 M	L	+	+	Chronic pyelonephritis	Malaria

^a L = lepromatous; B = borderline; T = tuberculoid.

^b ENL = erythema nodosum leprosum.

^c + = present.

^d - = absent.

^e GN = glomerulonephritis.

^f ATN = acute tubular necrosis.

TABLE 2. Major infections in 133 necropsies.

Infection	No.
Tuberculosis	
Pulmonary, alone or with hilar nodes	12
Lymph node only	10
Single organ (nonpulmonary)	2
Disseminated	12
Total	36
Cardiac infections	
Infective endocarditis	8
Myocardial abscesses	6
Acute pericarditis	1
Total	11
Nontuberculous pulmonary infections	
Bronchopneumonia with abscesses	12
Bronchopneumonia without abscesses	41
Lobar pneumonia	8
Chronic lung abscess	9
Total	70
Intracranial infections	10
Kidney abscesses	12
Pyemia	17

carditis. The cases of diffuse extracapillary and mesangiocapillary glomerulonephritis had advanced disease with many obsolescent glomeruli.

Multiple pyemic abscesses were seen in 12 patients as a secondary complication of severe infection in other sites, such as the endocardium or lung. The kidneys were enlarged and contained aggregates of neutrophilic leukocytes forming discrete abscesses, often involving glomeruli and with pus cell casts in the tubules. The inflammation destroyed large areas of renal parenchyma, and the patients had elevated blood urea levels. Three patients also had focal proliferative glomerulonephritis.

Fibrin deposits were present in the glomeruli and small arterioles in 10 patients, and were associated with an histologically identifiable, acute tubular necrosis in 8 cases. Acute tubular necrosis was difficult to diagnose in the presence of autolysis, but fibrin deposits were easily seen. Patient no. 35 developed acute tubular necrosis following ingestion of a poisonous plant. In the remaining patients renal failure was associated with septicemia.

Amyloidosis involving glomeruli and blood vessels was present in 10 patients, 9 of whom had lepromatous leprosy. All pa-

tients with amyloidosis had renal involvement. Other than the kidney, the liver, spleen and adrenals were common sites of amyloid deposition. The patients had proteinuria and nephrotic syndrome with or without elevated blood urea levels.

Chronic pyelonephritis was present in 5 patients who had uremia and irregularly scarred and contracted kidneys, showing tubular atrophy, interstitial fibrosis and chronic inflammation with relatively well-preserved glomeruli. The renal calyces in these patients were scarred and chronically inflamed. These changes were distinct from the small, wedge-shaped areas of subcapsular scarring found in most of the older patients and which were not considered significant lesions. Case 46 had traumatic paraplegia with cystitis and hydronephrosis.

Trophic ulcers were more common in the 50 cases with renal disease (Table 1) than in the rest of the patients ($p < 0.001$). There was also a statistically significant association between the presence of trophic ulcers and renal abscesses ($p < 0.01$), but this association could not be shown with other renal lesions.

Incidental and miscellaneous renal lesions included 4 cases of diabetic intercapillary glomerulosclerosis, 2 cases with vacuolar nephropathy due to electrolyte imbalance, 2 cases with miliary tubercles involving the kidney, and 1 case with adult-type polycystic renal disease. A metastasis from a thyroid carcinoma was present in 1 case. Medullary fibromas were seen in 2 cases, hemangiomas in 2 cases, and a small papillary adenoma in 1 case.

Infectious diseases. Bacterial infections other than leprosy (Table 2) were the major cause of mortality in 58 cases and of the remaining patients, only 19 had no infection at autopsy. Thirty-six patients had tuberculosis. Infective endocarditis present in 8 cases affected normal valves in 4 cases and was secondary to chronic rheumatic valvulitis in 3 cases and syphilitic aortitis in 1 case. Six patients had abscesses in the myocardium; in 4 of these, it accompanied endocarditis. Intracranial infections included pyogenic meningitis in 5 cases and multiple cerebral abscesses with or without cerebellar and meningeal involvement in 5 patients. Pyemia was diagnosed in 17 patients by the presence of multiple abscesses in

many organs. Two patients had gangrene of the leg.

Severe pyogenic infections were more common in patients with trophic ulcers than in the rest of the patients ($p < 0.05$). This association was most marked in severe pyogenic pulmonary infections ($p < 0.001$).

Tissue parasitic diseases encountered included amebic colitis in 2 patients; 1 of whom also had liver involvement and the other, colonic perforation and peritonitis. Filariasis was present in 4 patients and malaria, cerebral cysticercosis and strongyloidosis in 1 case each.

There were 3 cases of gastro-esophageal mucosal candidiasis. None of the others showed fungal infections, and there were no detectable viral infections except for viral hepatitis in 1 patient.

Visceral leprous granulomas. Foam cell granulomas with varying numbers of leprosy bacilli were present in the viscera of 41 patients distributed as follows: liver, 36 cases; spleen, 18 cases; adrenals, 17 cases; testis, 16 cases; and lymph node, 13 cases. Granulomas were occasionally seen in the myocardium, small intestine, and lungs, but kidney involvement was not encountered.

Other important lesions. Other causes of death included malignant neoplasms in 15 patients: squamous cell carcinoma of the skin in 5 patients, hepato-cellular carcinoma in 2, carcinoma of the lung in 2, gastric adenocarcinoma in 2, and carcinoma of the thyroid, Hodgkin's disease, adenocarcinoma of the gall bladder, and adenocarcinoma of the pancreas in 1 patient each.

Recent myocardial infarction had occurred in 1 patient, and 2 others had evidence of healed myocardial infarctions.

DISCUSSION

Many post-mortem studies of leprosy patients deal only with specific leprous lesions and amyloidosis. Some reports indicate in passing that "nephritis" (3, 18, 22), tuberculosis (3, 18), and septicemia (18) were important causes of death. Four reports, those of Kean and Childress (16) from Panama, Junnarkar (15) and Desikan and Job (11) from India, and Bernard and Vazquez (2) from Argentina, give details of general post-mortem findings. These include the presence of infective endocarditis and pericarditis (15, 16), severe pulmonary infections (2, 11, 15, 16),

pyelonephritis (2, 11, 16), multiple septic infarcts (16), and pulmonary and disseminated tuberculosis (2, 11, 15, 16). Our present study confirms the high prevalence of tuberculosis and also emphasizes the less well-known finding of frequent pyogenic infections (16) in these patients.

Infections were more common in necropsies on leprosy patients than in those on patients from the general medical wards of this hospital. However, the leprosy patients were from a more disadvantaged, poorer socioeconomic group from which controls were not available in sufficient numbers to allow meaningful statistical comparison. Although the disturbed immunity known to be present in leprosy (5) may play a part in promoting these infections, it is interesting that deep fungal infections were absent even though they are common in immunosuppressed patients in this geographical area (10). Infections were common in both lepromatous and nonlepromatous patients, and their occurrence did not appear to be influenced by the presence of ENL. There was a statistically significant association between the presence of trophic ulcers and severe pyogenic infections, especially pulmonary infections. This may be the result of dissemination of pyogenic organisms from secondarily infected ulcers.

Reports of renal biopsy findings in patients with leprosy have been reviewed recently (8). Three additional reports (6, 14, 20) are also available. Amyloidosis and glomerulonephritis are the best known renal lesions in leprosy. Amyloidosis was present in 7.5% of the patients in this study, and this value is near the median of the 0-14% prevalence reported in Indian patients with leprosy (6, 8, 20). Most of the cases had trophic ulcers and ENL. In some of our cases additional factors, such as tuberculosis and chronic lung abscesses, may have influenced the development of amyloidosis. Leprosy is a common cause of amyloidosis in this region (9).

Glomerulonephritis was seen in 11% of the patients. As may be expected in a study of necropsies, advanced stages of chronic irreversible forms of glomerulonephritis, such as the extracapillary and mesangio-capillary varieties, were relatively more common than in biopsy material (6, 8, 14, 20). Mesangial proliferative glomerulonephritis,

so commonly diagnosed in biopsies (^{6,8}), was less common, probably because minor degrees of mesangial hypercellularity are more difficult to identify in post-mortem material than in specially processed biopsies (⁸). The suggestion that glomerulonephritis in leprosy patients is multifactorial in etiology (⁸) is supported by its association with infective endocarditis (¹²) in four patients.

Pyogenic infections caused kidney damage by producing multiple renal abscesses in 12 patients and septicemia with intravascular coagulation in glomeruli and arterioles in nine cases. Acute tubular necrosis, probably resulting from ischemia due to microvascular obstruction, was present in seven of these cases. Acute tubular necrosis was not seen in two patients with intravascular fibrin deposits probably because death occurred before identifiable structural damage to the tubules could develop. There is only one previous report of acute tubular necrosis in leprosy (²³). This was in two patients in whom it was believed to have resulted from dapsone-induced intravascular hemolysis and intravascular coagulation (²³). Dapsone cannot be excluded as the cause of the acute tubular necrosis seen in the present study, but the presence of septicemia in most cases makes this unlikely. Papillary necrosis, the other reported renal complication of dapsone therapy (¹³), was not encountered. None of the patients had definite evidence of analgesic nephropathy, although small areas of medullary interstitial sclerosis of doubtful significance were seen in many cases.

There was a statistically significant association between the presence of trophic ulcers and the occurrence of major renal lesions. However, an association between ulcers and the different types of renal disease could not be demonstrated statistically, probably because of the relatively small number of cases of each type. It is possible that secondary infection of the ulcers by organisms such as streptococci could result in renal disease.

Malignant neoplasms were seen in 15 patients, only one of whom had a malignant lymphoma. In the absence of adequate controls, no definite statement about the risk of malignancy in leprosy can be made. However, it would appear that, as in other parts

of the world (⁴), leprosy patients do not have an increased risk of developing malignant lymphoma in spite of their depressed T cell function (⁵). Squamous cell carcinoma of the skin accounted for one third of all the cases of malignancy encountered, a much higher proportion than expected in Indians (¹⁹). This may be the result of the chronic trophic ulcers which afflict these patients. The low prevalence of myocardial infarction as a cause of death in this study correlates well with the absence of advanced atheromas in leprosy patients from this area (¹¹).

SUMMARY

A study of 133 necropsies on leprosy patients showed that renal disease, pyogenic infections, and tuberculosis were the most frequent causes of death. Major kidney lesions encountered included glomerulonephritis of different types, pyemic abscess, acute tubercular necrosis, amyloidosis, and chronic pyelonephritis. In many cases the renal lesions were secondary to infections in other organs.

Case control studies are required to determine if the high prevalence of these diseases is related to leprosy, its complications, or its therapy, per se, or if it is a reflection of the disadvantaged and poor socioeconomic status of these patients.

RESUMEN

Un estudio con 133 necropsias de pacientes con lepra reveló que las causas más frecuentes de muerte fueron enfermedad renal, infecciones piógenas, y tuberculosis. Las lesiones renales más frecuentes incluyeron glomerulonefritis de diferentes tipos, abscesos piémicos, necrosis, necrosis tubercular aguda, amiloidosis, y pielonefritis crónica. En muchos casos las lesiones renales fueron secundarias a infecciones en otros órganos.

Se requieren estudios sobre el control de los casos para determinar si la elevada prevalencia de estas enfermedades está relacionada con la lepra en sí, con sus complicaciones, con su terapia, o si es un reflejo del deficiente estado socioeconómico de los pacientes estudiados.

RÉSUMÉ

L'étude de 133 autopsies pratiquées chez des malades de la lèpre a révélé que les affections rénales, les infections pyogéniques, et la tuberculose constituaient les causes les plus fréquentes du décès. Les principales lésions rénales rencontrées comprenaient des glomérulonéphrites de différents types, des abcès pyohémiques, une nécrose tuberculaire aiguë de l'amyloïdose, ainsi que des pyélonéphrites chroniques. Dans

bien des cas, les lésions rénales étaient secondaires à des infections d'autres organes.

Il a fallu mener des études cas-témoins pour déterminer si la prévalence élevée de ces maladies étaient en relation avec la lèpre, ses complications, ou le traitement, ou bien s'il s'agissait d'une association avec le niveau socio-économique défavorisé des malades.

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