Study of Renal Changes in Leprosy[1]

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The presence of edema and proteinuria in lepra reaction has been noted. In India about 11.2% of the leprosy patients have been reported as dying of renal failure ([3, 9]). The exact histopathological lesions in the kidney and their nature is not clearly understood however. Most authors in their studies of renal changes in leprosy have reported nephritis of all types and amyloidosis in few cases ([1, 2, 3, 5, 7, 8, 9, 12, 13, 14, 16]). Specific lesions like lepromas have been reported by Powell and Swan in two of their 15 necropsies ([12]). Sainani and Rao ([13]) described the presence of leproma-like lesions composed of mononuclear cells with vacuolated cytoplasm without demonstrable acid-fast bacilli in one of their 60 cases. Most of the other workers have not reported such lesions.

In view of the high prevalence of the disease in this area it was thought worthwhile to study the renal changes in leprosy among our patients with special reference to the lepromatous type.

MATERIALS AND METHODS

This study was undertaken in 50 patients with leprosy of variable duration admitted to the leprosy ward during the period 1978–1979, in the General Hospital, Solapur.

Forty-five patients had lepromatous leprosy; while the remaining were of the tuberculoid (1), borderline (1), maculoanesthetic (1) and polyneuritic (2) type. Special attention was paid to the presence or absence of lepra reaction, the duration of the illness, and the duration of antileprosy treatment.

Patients with leprosy who also had pulmonary tuberculosis, diabetes mellitus, systemic hypertension, or congestive cardiac failure were excluded from the study.

The diagnosis of leprosy was made in all cases by thorough clinical examination, skin clip, and nasal smear for acid-fast bacilli (AFB) and was confirmed by skin biopsies. Urine examination for proteinuria, glycosuria and microscopy was done in every case. Blood urea, serum creatinine, blood sugar and serum proteins were estimated in each case. Every patient underwent percutaneous renal biopsy with the help of Franklin's modification of the Vim-Silvermann needle. The renal biopsy tissue was studied by hematoxylin and eosin staining, by Congo red staining for amyloid, and by the Fite-Faraco stain for AFB.

RESULTS

Of these 50 cases, 47 were males and 3 were females. The youngest patient was 18 years old and the oldest 60. Fifteen patients had leprosy of one to five years' duration; while the remaining 35 had had the disease for more than five years. Thirty-three patients had lepromatous leprosy with reaction; while 12 had lepromatous leprosy without lepra reaction. Five patients had non-lepromatous disease.

Twenty-five cases showed proteinuria. One patient presented with a nephrotic syndrome and the kidney biopsy ultimately showed amyloid changes. Out of these 25 cases with proteinuria, 21 patients were having lepra reaction. Blood urea and serum creatinine estimations were found to be within normal ranges in all cases.

The histopathologic features observed in these 50 cases are as shown in Table 1. Pathological changes were observed in 28 of the biopsies. The biopsies were unremarkable in the remaining 22 cases (Table 2). Relationships between serum proteins and the renal histology are shown in Table 3.

[1] Received for publication on 2 March 1981; accepted for publication in revised form on 16 November 1981.

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TABLE 1. *Histopathologic features observed in the 50 cases.*

Histopathologic changes	No. of cases (%)
A. Glomeruli	
1. Increase in cellularity of the capillary tuft	
a) Mild to moderate	3 (6)
b) Marked	3 (6)
2. Congestion	2 (4)
3. Hyalinization of glomerulus	– (–)
4. Periglomerular fibrosis	3 (6)
B. Tubules	
1. Cloudy change	25 (50)
2. Atrophy	3 (6)
3. Tubular hyaline-like cast	– (–)
C. Interstitial tissue	
1. Fibrosis	
a) Mild	10 (20)
b) Marked	10 (20)
2. Cellular infiltration (diffuse and local)	
a) Mild	6 (12)
b) Moderate	10 (20)
c) Marked	10 (20)
D. Vessels	
1. Arteriosclerosis	11 (22)
2. Wire-looping	4 (8)
E. Amyloid deposition	1 (2)
F. Acid-fast bacilli	– (–)

Abnormal renal histopathological findings were essentially present only in lepromatous cases and were usually associated with acute or chronic reactional states.

TABLE 2. *Renal histopathologic diagnoses and the clinical types of leprosy.*

Histopathologic lesion	Type of leprosy			Total
	LR[a]	L[b]	NL[c]	
Normal histology	10	8	4	22
Interstitial nephritis	8	1	1	10
Proliferative glomerulonephritis	6	–	–	6
Membranous glomerulonephritis	2	–	–	2
Amyloid	–	1	–	1
Cloudy change in tubules	21	4	–	25

[a] LR—Lepromatous leprosy with reaction.
[b] L—Lepromatous leprosy without reaction.
[c] NL—Nonlepromatous.

TABLE 3. *Serum proteins and renal histology.*

Albumin/globulin ratio	No. of cases	Renal histology	
		Normal	Abnormal
1.5 to 2	5	4	1
1 to 1.5	18	6	12
0.5 to 1	27	12	15
Total	50	22	28

One borderline case who showed interstitial nephritis also had a past history of lepra reaction. Interstitial nephritis (20%) and membranoproliferative glomerulonephritis (16%) were the most common lesions. Two cases (4%) showed interstitial scarring with sparse mononuclear cell infiltration mimicking a granulomatous lesion. However, these lesions were negative for AFB. Amyloidosis was found in one case (2%). Nonspecific cloudy change in the renal tubules was also present in 25 cases (50%).

DISCUSSION

Interstitial nephritis was seen in a large number of the cases in this study. It was indicated by varying amounts of tubular degeneration, foci of chronic inflammatory cells, and fibrosis in the interstitium. An association with lepra reaction was noted in nine of these ten cases. Similar observations have been made by Desikan and Job ([3]), Drutz and Gutman ([4]), Manson-Bahr ([11]), Sainani and Rao ([13]), and Gupta, *et al.* ([6]). However, Johny and Karat ([7]) did not encounter a single case of interstitial nephritis in their series of 60 cases. In the present study, proliferative glomerulonephritis and membranous glomerulonephritis were the next most common finding after interstitial nephritis, being noted in eight of the cases (Fig. 1).

In addition to these inflammatory changes, a few unusual observations were made, namely, intercapillary glomerulosclerosis (3 cases), periglomerular fibrosis (3 cases) and wire looping of blood vessels (4 cases). The wire looping of vessels could be caused by an immunological reaction. However, further immunological studies with electron microscopic observations would be needed to substantiate this hypothesis.

All these changes are nonspecific for leprosy. Nevertheless, they may indicate that leprosy predisposes the kidney to bacterial invasion by altering the immunological response of the host or by some other mechanism. Shwe and Jopling ([15]) performed immunofluorescent studies on kidney biopsies from seven patients with lepromatous leprosy and proteinuria. Granular deposits of immunoglobulins and complement were found in three of that seven suggesting an immune-complex pathogenesis.

In the present study, the two cases showing interstitial scarring mimicking granuloma are of interest. Reviewing the literature, we did not encounter any report of bacteriologically proven granuloma in the kidney. However, it is worth mentioning that a leproma without AFB was described by Sainani and Rao ([13]) in one case. Powell and Swan ([12]) and Mitsuda and Ogawa ([10]) also report occasional lepromas in their autopsy studies. In the present study, the absence of AFB may be explained by the prolonged treatment of all these patients with dapsone. Lepromas are commonly seen in the liver, the spleen and the testes, but their occurrence in the kidney is rare. The reason for such a small incidence is not known. Gupta, *et al.* ([6]) have postulated a relatively greater resistance of renal tissue to *M. leprae*.

Secondary amyloidosis was observed in one case (Fig. 2). It was confirmed by Congo red staining and polarized light microscopy which showed green birefringence. The rectal and gum biopsies of this patient were negative for amyloid. Kean and Childress ([8]) found renal amyloidosis in four cases out of 103 autopsies. Grabstald and Swan ([5]) and Powell and Swan ([12]) observed very high incidences of renal amyloidosis in their autopsy studies (46%). Johny and Karat ([7]) found three cases of amyloidosis in their series of 60 biopsies. Sainani and Rao ([13]) report one case out of 66 studied. Gupta, *et al.* ([6]) found no cases from their series of 50 patients.

This study has revealed that multitudes of pathologic alterations develop in the kidney in individuals suffering from chronic leprosy. None of the changes are specific or pathognomonic of leprosy. The changes appear to result from the interplay of bacillary products and immunologic factors.

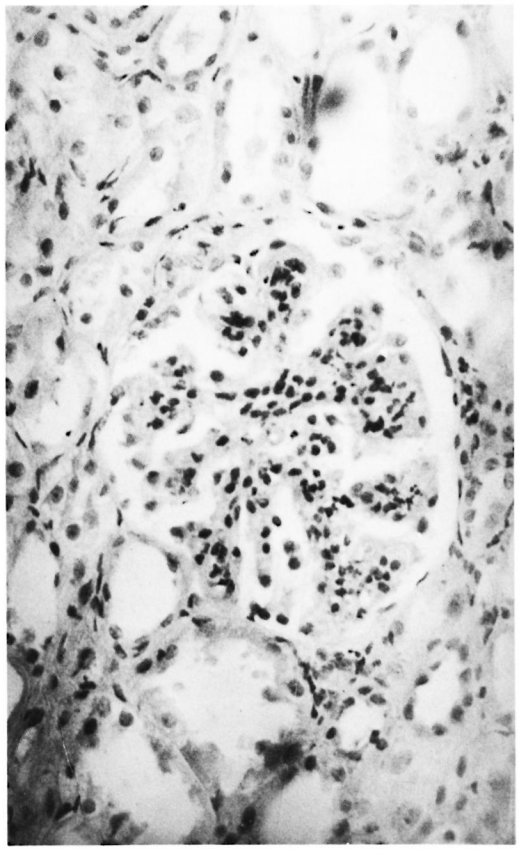

FIG. 1. Glomerular cell proliferation in a case of proliferative glomerulonephritis (H & E ×160).

Most lepromatous leprosy patients have an excess of serum gamma globulins combined with a deficit of specific cell-mediated immune responses. It is understandable that these excess antibodies may be forming complexes with bacterial products and may thus be responsible for changes such as membranous nephritis. Further involvement and activation of complement factors may explain the genesis of acute proliferative renal lesions, synovial lesions, and possibly the entire clinical gamut of the so-called lepra reaction. Amyloidosis in leprosy, although rare, also appears to be of the secondary type which follows prolonged immunological stimulation such as that seen in other chronic diseases such as tuberculosis.

The interstitial nephritis appears to be the result of secondary bacterial infection following an immunological insult due to the lepromatous process. Specific lepromas

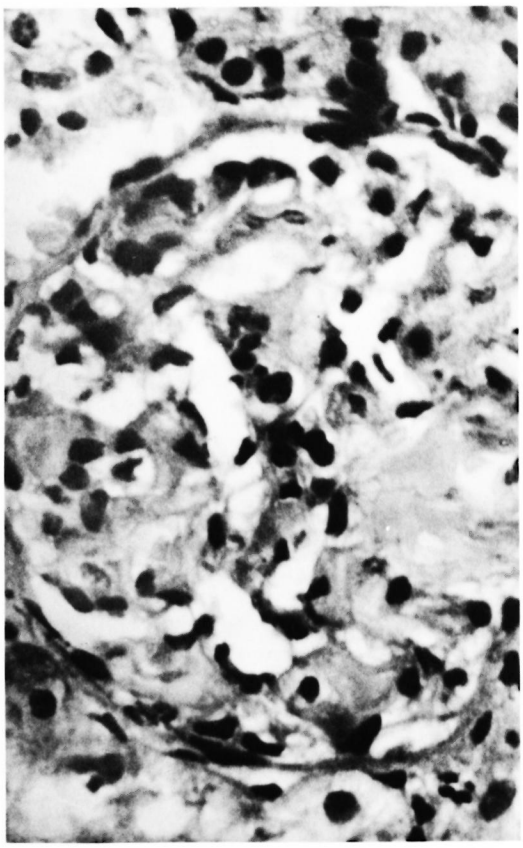

FIG. 2. Amyloid deposition in the glomerulus (H & E ×400).

suggestive of leprous interstitial nephritis seem to be extremely rare. Some of the interstitial nephritis may, however, be nonbacterial, and here the role of prolonged exposure to drugs such as dapsone has to be considered.

In conclusion, the present study shows a variety of renal lesions resulting from the interplay of various factors. Such changes would predictably complicate the clinical course of a patient with leprosy. With repeated insults of a) near toxic dosage levels of drugs, b) secondary bacterial infections, and c) immune complex formations as in lepra reaction, the renal lesions would be expected to progress and worsen. It is not, therefore, surprising that as many as 11.2% of leprosy patients ultimately go into renal failure.

These findings have a bearing on the management of leprosy. We suggest that in every chronic case of leprosy, treatment schedules should be carefully monitored to minimize the occurrence of lepra reactions and, should such lepra reactions develop, they should be controlled as quickly as possible. While monitoring serum gamma globulin levels, if it is felt that antibody has reached menacing levels, it is worth considering reducing the gamma globulin levels by a) plasmapheresis, b) suppression of B lymphocyte activity by steroids, or c) administration of cytotoxic immunosuppressive drugs for short periods under controlled conditions. These measures may help reduce the risk of renal involvement in leprosy.

SUMMARY

Renal lesions observed in 50 cases of chronic leprosy are reported. They include membranous and membranoproliferative glomerular lesions and amyloidosis forming one type possibly resulting from immune complexes. They also include lesions like chronic interstitial nephritis resulting from opportunistic secondary infections and/or drug toxicity. The evaluation of these lesions is discussed and appropriate remedial measures are suggested in the management of leprosy.

RESUMEN

Se hace un informe sobre la existencia de lesiones renales en 50 casos de lepra crónica. Estas lesiones incluyen alteraciones glomerulares membranosas y membranoproliferativas, así como un tipo de amiloidosis quizá resultante del depósito de complejos inmunes. También se incluyen lesiones como la nefritis crónica intersticial resultante de infecciones secundarias por oportunistas o por citotoxicidad de las drogas. Se discute sobre la evaluación de estas lesiones y se sugieren medidas para el manejo apropiado de la lepra.

RÉSUMÉ

On décrit les lésions rénales observées dans 50 cas de lèpre chronique, à savoir des lésions glomérulaires membraneuses et membrano-prolifératives, ainsi que l'amyloidose, qui pourrait consituter une catégorie à part résultant de la formation de complexes immuns. On a également inclus dans cette étude des lésions telles que celles qui résultent d'une néphrite chronique interstitielle, à partir d'infections secondaires ou de toxicité médicamenteuse. L'évaluation de ces lésions est discutée. On suggère des mesures appropriées pour y remédier, qui devraient être instituées dans le cadre de la lutte contre la lèpre.

Acknowledgment. We are grateful to the Dean, Dr. V. M. Medical College, Solapur, for permission to publish these data.

REFERENCES

1. ATTA, A. G., FLEURY, R. N., MARINGONI, R. L., TRINDADE, A. S., JR., RUFINO, C. B. F. and FILHO, B. S. Renal amyloidosis in leprosy. Int. J. Lepr. **45** (1977) 158–166.
2. BRUSCO, C. M. and MASANTI, J. G. Causes of death of leprosy patients, influence of lepra reactions and renal diseases. Int. J. Lepr. **31** (1963) 14–25.
3. DESIKAN, K. V. and JOB, C. K. A review of post-mortem findings in 37 cases of leprosy. Int. J. Lepr. **36** (1968) 32–44.
4. DRUTZ, D. J. and GUTMAN, R. A. Renal manifestation of leprosy: glomerulonephritis, a complication of erythema nodosum leprosum. Am. J. Trop. Med. Hyg. **22** (1973) 496–502.
5. GRABSTALD, H. and SWAN, L. Genitourinary lesions in leprosy with reference to the problem of atrophy of testis. JAMA **149** (1952) 1287–1291.
6. GUPTA, J. C., DIWAKAR, R., SINGH, S., GUPTA, D. K. and PANDA, P. K. Histopathologic study of renal biopsies in 50 cases of leprosy. Int. J. Lepr. **45** (1977) 167–170.
7. JOHNY, K. V. and KARAT, A. B. A. Renal biopsy studies in cases of leprosy. J. Assoc. Physicians India **19** (1971) 117–118.
8. KEAN, B. H. and CHILDRESS, M. E. A summary of 103 autopsies on leprosy patients on the Isthmus of Panama. Int. J. Lepr. **10** (1942) 51–59.
9. KRISHNAMURTHY, S. and JOB, C. K. Secondary amyloidosis in leprosy. Int. J. Lepr. **34** (1966) 155–158.
10. MITSUDA, K. and OGAWA, M. Study of 150 autopsies on cases of leprosy. Int. J. Lepr. **5** (1937) 53–60.
11. MANSON-BAHR, P. *Manson's Tropical Diseases*, 15th ed. London: Balliere Tindall, 1960, p. 531.
12. POWELL, C. S. and SWAN, L. L. Leprosy pathologic changes observed in 50 consecutive necropsies. Am. J. Pathol. **31** (1955) 1131–1147.
13. SAINANI, G. S. and NARAYAN RAO, K. V. Renal changes in leprosy. J. Assoc. Physicians India **22** (1974) 659–664.
14. SATYANARAYANA, B. V., RAJU, P. S., KUMARI, K. R., and REDDY, C. R. R. M. Amyloidosis in leprosy. Int. J. Lepr. **40** (1972) 278–280.
15. SHWE, T. and JOPLING, W. H. Bacteriuria, chronic phelonephritis and leprosy. Int. J. Lepr. **40** (1972) 318–320.
16. SHUTTLEWORTH, J. S. and ROSS, S. H. Secondary amyloidosis in leprosy. Ann. Intern. Med. **45** (1956) 23–28.