

## Autopsy Findings in 35 Cases of Leprosy in Malaysia<sup>1</sup>

Pailoor Jayalakshmi, Lai Meng Looi, Kuan Joo Lim,  
and Krishnan Rajogopalan<sup>2</sup>

Leprosy is still a public health problem in Malaysia, although the incidence is gradually declining. On the basis of data in the Registry of the National Leprosy Control Centre, the incidence is estimated to be about 4 per 100,000 population. Papers on leprosy from Malaysia have concentrated on the epidemiology, clinical manifestations and response to therapy. However, there is no study based on autopsy findings. The purpose of this paper is to highlight the pathological findings observed at autopsy on leprosy patients and to consider their clinical significance.

### MATERIALS AND METHODS

During the 5-year period between January 1981 and December 1985, autopsies were performed on 35 leprosy patients in the University Hospital, Kuala Lumpur. The subjects in this study were inmates of the leprosarium at the National Leprosy Control Centre, Sungai Buluh, Selangor. Mainly unclaimed bodies from the leprosarium were sent for post-mortem examination. At autopsy the gross findings were noted. Representative sections from the major organs, including normal and abnormal areas, were fixed in 4% buffered formaldehyde and embedded in paraffin. Sections were routinely stained with hematoxylin and eosin (H&E). Sections from the skin, nerve, liver, spleen, kidney and adrenals were stained by Fite's modification of the Ziehl-Neelsen stain for the detection of *Mycobacterium*

*leprae*. In addition, sections from at least one and frequently all of four organs, i.e., the heart, kidney, liver, and spleen, were stained with alkaline Congo red and examined for the presence of amyloid. Amyloid was defined according to the accepted histological criteria of Congophilia with green birefringence under cross-polarized light. All paraffin blocks of positive cases were further sectioned and stained with Congo red, and the extent of amyloid involvement was studied. Clinical data was obtained from case records. The classification of leprosy was based on clinical findings, skin smears and/or skin biopsies performed previously. Tuberculoid leprosy included the categories of borderline tuberculoid and polar tuberculoid leprosy. Similarly, lepromatous leprosy included borderline lepromatous and polar lepromatous cases. Statistical analysis of the autopsy data was done using the Chi-squared test.

### RESULTS

The ages of the patients at death ranged from 52 to 92 years with a mean age of 74 years. Thirty patients were Chinese and five were Indians. The majority (31) of patients were males. The clinical duration of the disease varied from 10 to 30 years. Twenty-three (66%) patients had lepromatous leprosy and 12 (34%) had tuberculoid leprosy.

**Infections.** Infections were common findings in this study. Pyogenic bronchopneumonia was seen in 12 (34%) cases and was the cause of death in six (17%) cases. Two patients had septicemia, one of whom had ascending cholangitis while the other developed a brain abscess. Nonspecific colitis with dehydration was noted in three patients. The prevalence of pulmonary tuberculosis was high, being detected in 10 (28%) cases, 3 of whom had caseating granulomata and 2 showed tuberculous bronchopneu-

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<sup>2</sup> P. Jayalakshmi, M.R.C.Path., Lecturer, and L. M. Looi, M.R.C.Path., M.R.C.P.A., Professor, Department of Pathology, Faculty of Medicine, University of Malaya, 59100 Kuala Lumpur, Malaysia. K. J. Lim, M.P.H., Deputy Director, and K. Rajagopalan, F.R.C.P., Director, National Leprosy Control Centre, Sungai Buluh, Selangor, Malaysia.

Reprint requests to Dr. Jayalakshmi.

TABLE 1. Renal lesions found at autopsy in 35 leprosy patients.

Pathology	Type of leprosy			
	Lepromatous (N = 23)		Tuberculoid (N = 12)	
	No.	%	No.	%
Interstitial nephritis	7	30	3	25
Glomerulonephritis	3	13	1	8
Pyelonephritis	4	17	2	17
Amyloidosis	5	22	1	8
Hypertension	3	13	1	8
Cortical cysts	—	—	1	8
No significant pathology	6	26	4	33

monia. Pulmonary aspergillosis in a tuberculous cavity was observed in one case. Four cases showed apical fibrosis and pleural adhesions suggestive of healed tuberculosis.

**Cardiovascular lesions.** Significant ischemic heart disease with fibrosis was noted in 11 subjects, and six had evidence of recent myocardial infarction. Left ventricular hypertrophy consistent with hypertension was noted in the remaining five cases. In addition, 34 patients had moderate-to-severe atherosclerotic changes in the coronary arteries and aorta.

**Renal lesions.** Kidney weights ranged from 40 g to 210 g, with average weights of the right and left kidney being 102 g and 108 g, respectively. Renal pathology occurred frequently and was observed in 24 cases. The various pathological changes detected in the kidneys are summarized in Table 1. Of note is the frequent occurrence of interstitial nephritis.

**Neoplasms.** Six patients had neoplastic lesions. The neoplasms were: carcinoma of the lung (2), moderately differentiated adenocarcinoma of the stomach with spread into the pancreas (1), leiomyoma of the stomach (1), adenocarcinoma of the prostate (1), and glioblastoma multiforme (1). Lymphoma or squamous cell carcinoma of the skin were not present in this series.

**Other important lesions.** There were five cases of gastroduodenal ulcers in this series; two of these perforated and contributed to the demise of the patients. The liver showed fatty change in six cases. There was one case of ascending cholangitis. The histology of the liver in seven cases showed infiltration

TABLE 2. Causes of death in 35 leprosy patients.

Disease	No.	%
Infections	14	40
Bronchopneumonia (6)		
Tuberculous bronchopneumonia (3)		
Infective colitis (3)		
Septicemia (2)		
Cardiac failure	7	20
Renal failure	6	17
Malignancies	4	11
Carcinoma of the lung (2)		
Glioblastoma multiforme (1)		
Carcinoma of the stomach (1)		
Intracerebral hemorrhage	2	6
Perforated peptic ulcer	2	6
Total	35	100

of the portal tracts by moderate numbers of lymphocytes. However, no lepromas were noted. Gallbladder calculi were present in six patients. There were two cases of intracerebral hemorrhage. The testes were examined histologically in ten cases and showed atrophy in four. The lymph nodes, thyroid, and adrenals did not show significant pathology in any of the cases.

**Lepromas.** No lepromas were noted in the visceral organs. Fite's stain on sections from the spleen, kidney, liver, and adrenals did not reveal leprosy bacilli.

**Skin and peripheral nerves.** Deformities of the hands and feet, such as shortening of the fingers and loss of toes, were seen in 31 (89%) cases. Trophic ulcers in the feet were seen in ten (28%) cases, of which eight had lepromatous leprosy. Bedsores in the sacral region were noted in nine (26%) patients. None of the patients had active skin lesions at the time of post-mortem examination. Sections of the skin were taken in 11 cases, of which 7 were normal and 4 showed a few foam cells around the dermal appendages. Fite's stain did not show leprosy bacilli in these. Thickened ulnar and popliteal nerves were noted in 20 (57%) cases. Sections from the ulnar or popliteal nerves were taken in 12 of these cases; 6 showed fibrosis and 6 showed no significant pathology. No granulomas were noted, and the Fite's stain showed no organisms.

**Amyloidosis.** Generalized amyloidosis was observed in 6 (17%) patients, of whom 5 had lepromatous leprosy and 1 had tu-

berculoid leprosy. The major organs involved were the heart (100%), kidney (100%), adrenals (100%), liver (83%), spleen (83%), and lungs (83%). In the heart, amyloid was deposited in the reticulin of the myocardium as well as in the intra-myocardial vessels. Amyloid deposition in the kidney frequently involved the glomeruli, vessels as well as tubular basement membrane. Besides vascular involvement, amyloid was occasionally seen in the sinusoids of the spleen and along the alveolar septa of the lung. In most of the organs involved, the deposits were essentially limited to the walls of medium-sized arteries. An exception was the brain which was totally spared.

**Causes of death.** The causes of death are listed in Table 2. Infection, particularly bronchopneumonia, was the most common. The other major causes of death were cardiac and renal failure. It appears that leprosy per se was not a significant cause of death in this series.

#### DISCUSSION

The National Leprosy Control Centre at Sungai Buluh, Selangor, supervises and coordinates leprosy control activities in Malaysia. It consists of a hospital of 855 beds (815 leprosy beds and 40 general beds), an old leprosy settlement of 2000 bed chalets, a research unit, and an administration block. The racial distribution of the inmate population shows 10.5% Malays, 82.2% Chinese, 5.8% Indians, and 1.5% others. The data suggest a relatively higher prevalence of leprosy among Chinese in view of the fact that Chinese constitute only 32% of the general Malaysian population. The reasons are controversial. The true incidence may not be as high as what is indicated, because the Chinese tend to seek modern medical treatment more readily than Malays or Indians.

The majority (71%) of the inmate population have lepromatous leprosy. This is due to the fact that patients with lepromatous leprosy are more infectious and are hospitalized for long periods. The patients in this study have been inmates of the hospital for many years. Available for autopsy are mainly unclaimed bodies, mainly Chinese and Indians. Malays are underrepresented because permission for autopsy was frequently not granted by the relatives on cul-

tural or religious grounds. Because of this factor of selection, the observations in this study may not be representative of all the leprosy patients of the Centre. In spite of these limitations, this study is still useful in providing information regarding the pathological changes in Malaysian leprosy patients.

Infection was the most important cause of death in the present study. Bronchopneumonia was the most common pathological entity. The high prevalence of infection may be related to poor resistance of leprosy patients to organisms (<sup>2</sup>). In addition, the high age of the patients and the presence of trophic ulcers and bedsores are likely contributory factors. However, we were not able to demonstrate a statistically significant association between the presence of trophic ulcers and pyogenic infection. An association may become evident if more cases are studied. Such an observation was made by Date, *et al.* (<sup>3</sup>).

Tuberculosis was an important associated disease in the present study. Our finding is not surprising since it is well known that the prevalence of tuberculosis among leprosy patients is high. Liu and Qiu (<sup>6</sup>) from China and Mitsuda and Ogawa (<sup>7</sup>) from Japan have reported that tuberculosis was the cause of death in 23.3% and 54.7% of their leprosy cases, respectively.

Cardiac failure was present in seven patients and constitutes one of the major causes of death in our study. All cases had moderate-to-severe atherosclerosis with calcification of the plaques. These findings are consistent with those of Bernard and Vazquez (<sup>1</sup>). In contrast, Desikan and Job (<sup>4</sup>) noted a low incidence of atheromatous lesions in the aorta. The reasons given by them were poor nutritional status and hormonal imbalance due to testicular atrophy. The majority of the patients in our study were well nourished and were, hence, not spared from atherosclerosis. There was no significant relation apparent between the presence of atherosclerosis and ethnic group.

Powell and Swan (<sup>9</sup>) found leprosy bacilli in the tissues in 6 out of 10 patients who were considered to be clinically arrested. The common organs involved were the liver, spleen, and adrenals. It is interesting to note in our study that no lepromas were observed

and no bacilli detected in the visceral organs. This is probably due to the fact that the subjects studied were "burned out" cases.

Changes in the kidneys were noted in 25 (71%) patients and contributed to the high morbidity. Interstitial nephritis appeared to be the most commonly observed lesion. Similar observations have been made by others<sup>(5,8)</sup>. The renal changes may be due to altered immunity with increased susceptibility to infection. Alternatively, drug reaction, related to prolonged exposure to sulfones, may have a role to play. The high prevalence of renal changes observed indicate that it would be worthwhile to look for such lesions in leprosy patients in order to prevent unnecessary morbidity.

With regard to screening for amyloidosis, not all of the cases were handled identically. Although most patients had four organs (heart, liver, kidney, and spleen) screened with Congo red, there were some who had fewer organs screened. As such, the figure of 17% is not a true incidence. It can be inferred, however, that the prevalence is at least 17% since a more stringent screening could only result in more cases. The morphological features and distribution of amyloidosis in this study are consistent with secondary systemic amyloidosis. Amyloidosis was observed in 5 (21.7%) out of 23 patients with lepromatous leprosy and 1 (8.3%) out of 12 patients with tuberculoid leprosy. This overall prevalence rate of 17% is high compared to that reported from India<sup>(4)</sup>, but is similar to observations from Western countries<sup>(7, 10, 11)</sup>. There has been no good explanation offered for the wide geographical variation in prevalence observed in various reports. The fact that most of our patients had lepromatous rather than tuberculoid leprosy is probably an important factor, since amyloidosis is known to complicate the lepromatous form of leprosy more frequently than other forms of the disease. However, an association between the prevalence of amyloidosis and lepromatous leprosy could not be demonstrated statistically in this study, probably due to the small number of cases. The study by Williams, *et al.*<sup>(12)</sup> suggested that higher animal fat consumption was accompanied by a higher risk of amyloidosis. Pras<sup>(10)</sup> pointed out that genetic makeup had a role to play. However,

the extent to which dietary or genetic factors have contributed to the high prevalence of amyloidosis in this study can only be speculative at this stage. The high prevalence observed, however, warrants awareness of the condition among personnel involved in the management of leprosy patients.

### SUMMARY

The findings of autopsies performed on 35 leprosy subjects in the University Hospital, Kuala Lumpur, between January 1981 and December 1985 are presented. This is the first report based on autopsy findings from Malaysia. The patients were elderly subjects with a mean age of 74 years. Sixty-six percent had lepromatous leprosy. None had active skin lesions. The most common cause of death was pyogenic infection, particularly bronchopneumonia. Tuberculosis was noted in 25% of the cases. The other important causes of death included cardiac and renal failure. Renal lesions were evident in 71% of the cases, and the most common pathology was interstitial nephritis. Generalized amyloidosis complicated six (17%) patients.

### RESUMEN

Se presentan los hallazgos de las autopsias efectuadas en 35 sujetos con lepra en el hospital universitario de Kuala Lumpur entre enero de 1981 y diciembre de 1985. Este es el primer reporte basado en los hallazgos de autopsias en Malasia. Los pacientes fueron individuos con un promedio de edad de 74 años. Sesenta y seis por ciento tuvieron lepra lepromatosa. Ninguno tuvo lesiones activas de la piel. La causa más común de muerte fue la infección piógena, particularmente bronconeumonía. En el 25% de los casos se encontró tuberculosis. Las otras causas importantes de muerte incluyeron fallas cardíaca y renal. Las lesiones renales fueron evidentes en el 71% de los casos y la patología más común fue nefritis intersticial. En 6 pacientes (17%) la enfermedad estuvo complicada por amiloidosis generalizada.

### RÉSUMÉ

On relate ici les observations faites au cours d'autopsies pratiquées chez 35 malades de la lèpre à l'hôpital universitaire de Kuala-Lumpur, entre janvier 1981 et décembre 1985. Ceci est le premier rapport basé sur des autopsies en Malaisie. Les malades étaient des sujets âgés, leur âge moyen étant de 74 ans. Soixante-six pour cent souffraient de lèpre lépromateuse. Aucun ne présentait de lésions cutanées actives. Des infections pyogéniques, et particulièrement la bronchopneumo-

nie, constituait la cause habituelle du décès. Une tuberculose a été notée chez 25% des cas. Les autres causes importantes de décès comprenaient la décompensation cardiaque ou rénale. Des lésions rénales ont été relevées chez 71% des cas, la pathologie la plus commune étant la névrite intersticielle. Six (17%) de ces malades présentaient comme complication une amyloïdose généralisée.

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