# Amyloidosis in Leprosy[1]

Motoaki Ozaki and Mutsuhiro Furuta[2]

It is well known that systemic amyloidosis is frequently associated with leprosy. In Japan, Inaba ([11]) reported 7.8% incidence of secondary amyloidosis among 268 leprosy patients autopsied between 1938 and 1945, i.e., in the pre-chemotherapeutic era. Sasaki and Kawatsu ([25]) observed an increase of secondary systemic amyloidosis associated with leprosy, based on autopsy findings of 200 cases between 1955 and 1970. Recent studies indicate that the immune system plays a more important role in amyloid pathogenesis than previous studies indicated. Amyloidosis in leprosy patients has been interpreted as being secondary to leprosy, but it involves more complicated problems than such a simple interpretation suggests. We studied systemic amyloidosis of leprosy histopathologically in 160 autopsy cases from two leprosaria in Japan. The purpose of this presentation is to report manifestations of amyloidosis associated with leprosy, referring to relations between amyloid deposits and other pathologic findings.

## MATERIALS AND METHODS

A total of 160 leprosy autopsies studied, conveniently fall into two groups. Group A consisted of 50 consecutive autopsy cases in the Kikuchi National Leprosarium, Keifu-en, from 1955 to 1959. This period corresponds to an early phase of antileprosy chemotherapy associated with the occurrence of clinical and bacteriologic improvement. Group B consisted of 110 autopsy cases in the Oku National Leprosarium, Komyo-en, from 1962 to 1971. The autopsy rate in this decade was 85.3%. In this group, the leprous lesions of most lepromatous cases were well subsided and quiescent.

Congo red stain and polarized microscopy are the best methods of determining the existence of amyloid deposits in tissues. The present study was mainly based on the use of these two procedures, though Thioflavin S and alcian blue stainings were also used in several cases. In some cases, amyloid deposits were limited to small blood vessel walls of one organ; such cases were also included among amyloid cases since the deposits were thought to be early and limited depositions of essentially systemic nature.

## RESULTS

Of 50 cases, in Group A, 23 cases (46%) showed amyloid deposits. In Group B, amyloid deposits were observed in 17 of 110 cases (15.4%). Clinicopathologic findings of these amyloidal cases are summarized in Tables 1 and 2. The type of leprosy is shown in Table 2; this classification is based on that of Japanese leprosaria, dividing leprosy into two types, lepromatous and tuberculoid. The lepromatous diagnosis probably covered LL, BL and BB; the tuberculoid, BT and TT ([24]). Microscopic examination was done mainly on visceral organs and in several

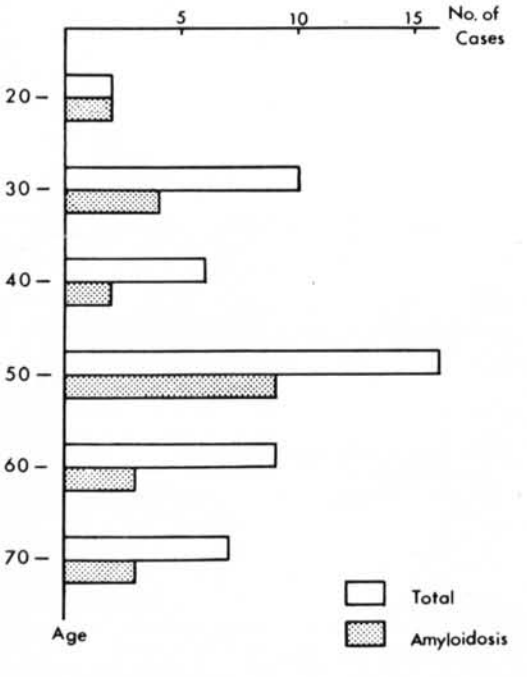


FIG. 1. Age distribution of amyloidal cases in Group A.

[1] Received for publication 18 April 1974.

[2] Motoaki Ozaki, M.D., Department of Chemotherapy, National Leprosarium, Nagashima Aisen-en, Okayama, Japan; Mutsuhiro Furuta, M.D., Chief Pathologist, Department of Pathology, Kyoto National Hospital, Kyoto, Japan. Address for reprints: M. Furuta, M.D., Department of Pathology, Kyoto National Hospital, Fushimi, Kyoto 612, Japan.

TABLE 1. *Details of amyloid cases in Group A.*

| No. | Age | Sex | Amyloid deposit | Main pathologic finding |
|---|---|---|---|---|
| KK55-1 | 31 | M | Spleen, kidney, adrenal, pancreas | Tuberculosis: lung & intestine.<br>Chronic pyelonephritis. |
| KK56-1 | 40 | M | Thyroid | Tuberculosis: lung, trachea & pharynx. |
| KK57-8 | 24 | M | Spleen, pancreas, urinary bladder | Tuberculosis: lung & intestine. |
| KK57-9 | 75 | M | Spleen, kidney, pancreas | Tuberculosis: lung & liver. |
| KK57-11 | 77 | M | Kidney | Gastric carcinoma. |
| KK57-12 | 51 | M | Kidney, pancreas, lung | Rectal carcinoma. |
| KK57-15 | 22 | M | Spleen, kidney, pancreas | Tuberculosis: lung, liver & spleen. |
| KK57-16 | 76 | M | Spleen | Lobar pneumonia. |
| KK57-17 | 30 | M | Spleen | Tuberculosis: lung, trachea & liver.<br>Banti's syndrome. |
| KK57-18 | 60 | M | Spleen, pancreas, thyroid | Aspirative pneumonia. |
| KK57-19 | 68 | M | Kidney | Aspirative pneumonia.<br>Chronic pyelonephritis. |
| KK58-2 | 74 | M | Spleen, kidney | Liver cirrhosis.<br>Bronchopneumonia. |
| KK58-3 | 57 | M | Spleen | Tuberculosis: lung. |
| KK58-4 | 55 | F | Spleen, kidney, pancreas | Suppurative cystitis.<br>Acute & chronic pyelonephritis.<br>Carcinoma of uterus. |
| KK58-7 | 58 | F | Spleen | Chronic pyelonephritis.<br>Accidental death. |
| KK58-8 | 48 | M | Spleen | Tuberculosis: lung. |
| KK58-9 | 64 | F | Spleen | Carcinoma of ovary.<br>Chronic pyelonephritis. |
| KK58-10 | 59 | M | Spleen | Lobar pneumonia.<br>Chronic pyelonephritis. |
| KK58-11 | 56 | M | Spleen | Fatty heart. |
| KK59-1 | 30 | M | Spleen, kidney, pancreas, lymph node | Acute & chronic pyelonephritis.<br>Infectious splenomegaly. |
| KK59-2 | 53 | F | Spleen | Hepatoma.<br>Liver cirrhosis. |
| KK59-3 | 52 | M | Spleen, kidney | Liver cirrhosis. |
| KK59-4 | 37 | M | Spleen, kidney, pancreas, intestine | Epicarditis.<br>Chronic pyelonephritis.<br>Infectious splenomegaly. |

Types of leprosy were not available in the original protocols.

cases lymph nodes were included. The most frequent organs involved were the kidney and spleen.

Clinical data of amyloidal cases are compared with that of nonamyloidal cases in Table 3. The incidence of amyloid deposits in male patients of Group A was significantly greater than in the female ($p < 0.05$). There was no predilection for either type of leprosy in Group B. As shown in Figures 1 and 2, amyloidosis was distributed irregularly in each age group. All cases in their

TABLE 2. *Details of amyloid cases in Group B.*

| No. | Age | Sex | Type[a] | Amyloid deposit | Main pathologic finding |
|---|---|---|---|---|---|
| OK62-2 | 35 | M | L | Spleen, kidney, pancreas, thyroid, heart | Chronic pyelonephritis. |
| OK62-14 | 25 | M | L | Spleen, pancreas, adrenal, thyroid | Bronchopneumonia.<br>Chronic pyelonephritis. |
| OK62-15 | 46 | M | T | Spleen, kidney, adrenal | Bronchopneumonia.<br>Acute enterocolitis. |
| OK63-4 | 70 | M | T | Kidney | Bronchopneumonia.<br>Chronic pyelonephritis. |
| OK63-5 | 64 | M | L | Kidney | Bronchopneumonia. |
| OK63-6 | 36 | M | L | Spleen, kidney, pancreas, liver, adrenal, thyroid, lung, heart, testis, lymph node | Chronic pyelonephritis. |
| OK63-8 | 55 | M | L | Spleen, kidney, pancreas, thyroid, lung, heart | Chronic pyelonephritis. |
| OK64-2 | 74 | M | T | Kidney, adrenal, thyroid | Chronic pyelonephritis.<br>Atelectasis, pulmonary. |
| OK64-5 | 51 | M | L | Kidney, adrenal | Bronchopneumonia.<br>Chronic pyelonephritis & cystitis. |
| OK64-9 | 51 | M | L | Thyroid | Chronic pyelonephritis.<br>Pulmonary infarction. |
| OK64-12 | 40 | M | L | Kidney, adrenal | Chronic pyelonephritis.<br>Acute & chronic hepatitis.<br>Hepatic abscess. |
| OK69-6 | 65 | M | T | Spleen, kidney, adrenal | Pyothorax.<br>Chronic pyelonephritis.<br>Occult carcinoma, prostate. |
| OK69-10 | 48 | M | L | Kidney, pancreas, | Tuberculosis: lung, liver & spleen.<br>Caseous pneumonia.<br>Chronic pyelonephritis. |
| OK70-1 | 84 | F | T | Spleen, kidney, pancreas, liver, adrenal, intestine, urinary bladder, brain | Hepatoma.<br>Chronic pyelonephritis & cystitis. |
| OK70-8 | 85 | F | L | Spleen, liver, adrenal, brain | Bronchopneumonia.<br>Acute cholecystitis.<br>Chronic pyelonephritis. |
| OK70-13 | 81 | M | L | Spleen, kidney, liver, thyroid | Gastric carcinoma.<br>Chronic pyelonephritis. |
| OK71-2 | 43 | F | L | Spleen, kidney | Pulmonary emboli. |

[a] L = lepromatous; T = tuberculoid.

twenties of both groups showed amyloid deposits (KK57-8, KK57-15, OK62-14). Two cases in Group A were associated with active pulmonary tuberculosis, involving intestines (KK57-8) or liver and spleen (KK57-15). One case of Group B (OK62-14) showed remarkable generalized amyloidosis; the causes of death were amyloid kidney and bronchopneumonia. There was no predilection of amyloid deposits for patients over 70 years of age. The average age of amyloidal cases was significantly lower than that of

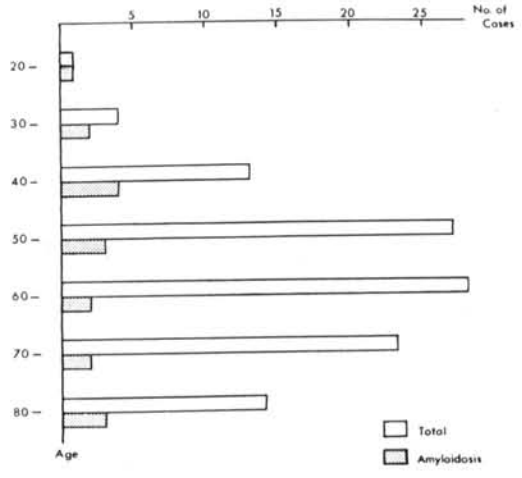


FIG. 2. Age distribution of amyloidal cases in Group B.

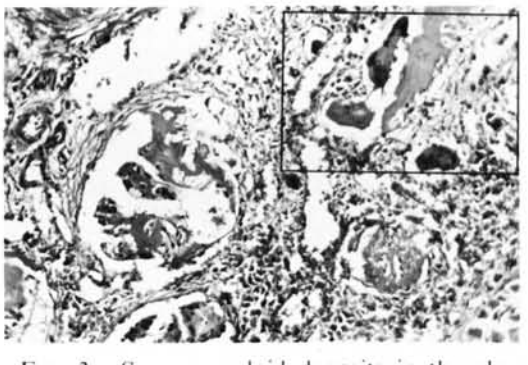

FIG. 3a. Severe amyloid deposits in the glomeruli and in the stromal space (KK57-15). Small round cell infiltration is seen in the stroma. H. E. ×140.

nonamyloidal cases in both groups ($p < 0.05$). Foreign body giant cells were observed in the amyloidal kidney of one case in Group A (KK57-15, Figs. 3 and 4).

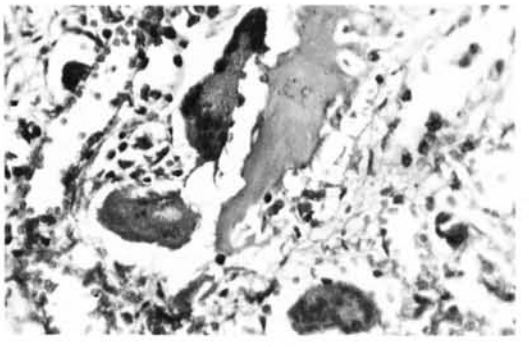

FIG. 3b. Higher magnification showing foreign body type multinuclear giant cells around the amyloid deposit. Amyloid substance is also present in the cytoplasm of these giant cells. H. E. ×280.

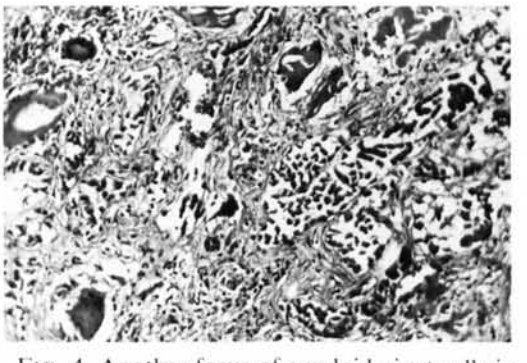

FIG. 4. Another focus of amyloid giant cells in the kidney (KK57-15). There are four distinct giant cells and massive tubular destruction. H. E. ×140.

## DISCUSSION

Amyloidosis associated with leprosy patients has been classified as secondary amyloidosis. This interpretation, however, seems too simple as it is not reasonable to regard all amyloidosis of leprosy patients as being

TABLE 3. *Differences between amyloid and non-amyloid cases.*

| | Group A | | | Group B | | |
|---|---|---|---|---|---|---|
| | Total | Amyloid | Non-amyloid | Total | Amyloid | Non-amyloid |
| No. of cases | 50 | 23 | 27 | 110 | 17 | 93 |
| male | 34 | 19 | 15 | 85 | 14 | 71 |
| female | 16 | 4 | 12 | 25 | 3 | 22 |
| Average age (yrs.) | 53.0 | 51.2 | 54.6 | 62.5 | 56.0 | 63.6 |
| Type[a]: L | — | — | — | 78 | 12 | 66 |
| T | — | — | — | 32 | 5 | 27 |

[a] Type: L = lepromatous; T = tuberculoid.

TABLE 4. *Complications of amyloid cases.*

| Complications | Group A | | Group B | |
|---|---|---|---|---|
| | Total | Amyloid | Total | Amyloid |
| No. of cases | 50 | 23 | 110 | 17 |
| Tuberculosis | 16 | 8 | 8 | 1 |
| Malignant tumor | 7 | 5 | 33 | 3 |
| Chronic pyelonephritis | 20 | 8 | 45 | 14 |

secondary to leprosy. Each leprosy patient with amyloid deposits usually has various different complications. From these complications we concentrated on three diseases: tuberculosis, malignant tumor and pyelonephritis. Table 4 shows the number of cases with these complications. Before chemotherapy spread in Japan, about half of the leprosy patients in leprosaria died of tuberculosis. Active tuberculosis was found in 16 of 50 cases of Group A (32%); half of them accompanied amyloidosis. Of Group B, eight cases (7.3%) showed active tuberculous lesions mainly in the lung; amyloid deposits were observed in only one of them. Tuberculous lesions of this case (OK69-10) involved the lung, liver, spleen, and lymph nodes. Severe pyelonephritis was also present. Though Lüders ([17]) reported correlation of tuberculosis with amyloidosis, we could not find a positive relation between them in this study.

Seven cases of Group A (14%) were associated with malignant tumors, five of which had amyloidosis. Myelomatosis or malignant lymphoma was not included in these cases with malignancy. Group B showed a greater incidence of malignant tumors, i.e., 33 of 110 cases (30%). Amyloid deposits were detected in three cases. They were cases of stomach carcinoma, hepatoma and occult prostatic carcinoma. Three lepromatous cases with malignant lymphoma did not show any amyloid deposit. According to a study by Azzopardi and Lehner ([1]) on 93 cases of systemic amyloidosis, 14 cases (15%) were associated with malignancy. Half of them had myelomatosis or malignant lymphoma. They emphasized a greater incidence of renal cell carcinoma among the other seven cases with carcinoma. Myelomatosis was not included in our cases of both groups and we could not determine any definite correlation of amyloidosis with renal cell carcinoma.

In both Groups A and B, about one third of the cases with pyelonephritis showed amyloid deposits. Mild chronic pyelonephritis was excluded from these cases in Table 4 since pathologic significance of such mild chronic pyelonephritis remains unknown. The incidence of amyloidosis in Group B significantly correlated with pyelonephritis ($p < 0.05$). Brownstein and Helwig ([2]) observed that suppurative pyelonephritis was the most frequent underlying disorder among chronic pyogenic infections; on the other hand, chronic pyelonephritis, frequent in routine autopsy, seldom complicated amyloidosis. Leprosy patients with sensory disturbance of extremities are always exposed to bacterial infection owing to ulcerating or traumatic lesions of the extremities. Pyelonephritis was the most common complication in the patients of the present study. However, chronic pyelonephritis in leprosy patients is usually neglected unless clinical findings become remarkable. The present study seems to suggest that amyloidosis of leprosy patients is related to renal disorder such as pyelonephritis.

The average age of Group B was about ten years older than that of Group A (Table 3). This is due to longer life span of nonamyloidal cases in Group B. Difference in the average age between nonamyloidal and amyloidal cases was statistically significant in both groups ($p < 0.05$). Association of amyloidosis distinctly shortens the life of a leprosy patient. Wright *et al* ([31]) recorded that the incidence of amyloid deposits was significantly greater in older patients. We were unable to find any increase of amyloid deposits in patients over 70 years of age. In frequency as well as in the histopathologic findings, the amyloid deposits of the present study differ from nonsystemic microdeposits of amyloid seen in the aged ([21]).

A predilection of amyloidosis for the lep-

romatous type is reported in the literature. We, however, could not come to any correlation between amyloidosis and leprosy type in Group B (Table 3). Lepromatous leprosy is generally regarded as having depressed cell-mediated immunity (CMI) and tuberculoid type as representing accelerated CMI. The present study does not give any evidence correlating this immunologic difference directly with amyloid pathogenesis. It is difficult to say whether leprosy should be regarded as a sequence of chronic infectious disease stimulation resulting in amyloid deposits or not. In lepromatous cases, tremendous numbers of bacilli may remain in the tissues for a long period. This may be interpreted as a cause of amyloid deposits. The present study, however, reveals a paradox in this assumption in that the incidence of amyloidosis during the era of chemotherapy was greater than that of the pre-chemotherapeutic period ([11]). This difference is not derived from difference of technical procedure. We should rather suppose that there has been some change in amyloid-inducing factors in these patients.

The greater incidence of amyloidosis in Group A might be related to the fact that the group consisted of cases from the relatively early stage of leprosy chemotherapy in Japan. An autopsy report from the U.S.A. also noted a high frequency of amyloidosis associated with leprosy patients during nearly the same period ([20]). It is generally said that antileprous agents have increased the frequency of lepra reactions such as *erythema nodosa leprosum* (ENL) or reversal reaction ([23]). Corticosteroids were not used to control these acute episodes during the period covered by Group A. Contreras *et al* ([3]) postulated that lepra reactions were related to amyloid pathogenesis and that corticosteroids enhanced the incidence and involvement of amyloid deposits. Cortisone has been included in the immunosuppressive agents used to induce amyloid deposits ([8]); however, the results of experimental amyloidosis by cortisone do not concur with each other ([19]). Treatment by various methods has been able to control more effectively the reactive stages in the clinical course of leprosy. That may be related to the lower incidence of amyloidosis in Group B, though available clinical records were too restricted to permit examination of the relationships of amyloidosis as to type, treatment and clinical course of leprosy in the patients studied.

Autopsy reports on amyloidosis of leprosy patients under chemotherapy are summarized in Table 5 ([4, 13, 20, 25, 26]). Remarkable variance of the incidence is observed through examinations of patients with the same disease in nearly the same period. Thus, it is supposed that many factors such as immunologic factors or race and social environment ([30]) may complexly influence the etiogenesis of amyloid deposits. Brownstein and Helwig ([2]) noted a decrease in amyloidosis in autopsy cases with leprosy in the U.S.A. If a detailed report is published, it would be profitable to compare it with the result of our study.

A study by Lendrum *et al* ([14]) indicates that their sodium sulfate-alcian blue method revealed aging of amyloid with loss of characteristic staining reactions. Their method

TABLE 5. *Autopsy reports on amyloidosis in leprosy patients.*

| Author | Country | No. of cases | Duration | Average age (years) | Amyloidosis |
|---|---|---|---|---|---|
| Powell and Swan (1955) | U.S.A. | 50 | 1948-54 | 58.8 | 23 (46.0%) |
| Schuttleworth and Ross (1956) | U.S.A. | 18 | 1952-55 | 62.2 | 10 (55.5%)[a] |
| Krishnamurthy and Job (1966) | India | 25 | 1953-64 | — | 2 ( 8.0%)[a] |
| Desikan and Job (1968) | India | 37 | 1941-64 | 35 | 4 (10.8%) |
| Sasaki and Kawatsu (1972) | Japan | 200 | 1955-70 | 56.1 | 21 (10.5%)[b] |

[a]All lepromatous.
[b]All lepromatous except one tuberculoid case.

was applied to several cases in our study, but we could not find any obvious evidence of amyloid aging. Amyloid would not deposit at the same time in various organs. In the present study, amyloid deposited most frequently in the kidney and spleen. When the deposit was found only in one organ, the kidney or the spleen was the most frequent organ. Thus, we may say that early amyloid deposit occurs in these organs. In the present study the site of early deposit in the spleen was in smaller arterial walls, which differs from the perifollicular deposition in the spleen of experimental amyloidosis. It seems that early amyloid deposits may occur first in the small arteries or arterioles of the spleen and the glomerular capillaries and small arteries or arterioles of the kidney. Eliakim and Rosenmann [5] reported a clinical case which presented the first amyloid deposits as being in the mesangial area of the glomeruli. The systemic deposit in the small arteries or capillary walls suggests the existence of some circulating factors.

The role of the reticuloendothelial system in amyloid pathogenesis has been emphasized [28]. Amyloid deposits of leprosy patients are possibly related to the reticuloendothelial system, but the local secretion theory cannot be applied to all sites with amyloid deposits. Renal complications were observed in many of the amyloidal cases of the present study. These might be caused from amyloidal changes of the kidney. Furthermore, renal changes by some complicating disorders might be an inducing factor in amyloid deposition in the kidney. The case reported by Eliakim and Rosenmann [5] indicates the possibility of renal amyloidosis originating from nonspecific glomerulitis. In lepromatous leprosy, glomerular changes in immunologically reactive stages such as ENL may be related to amyloid pathogenesis in the kidney.

There is a classification which distinguishes amyloidosis into two patterns of distribution, i.e., peri-reticulin and peri-collagen [10]. The present study revealed no significant difference by this classification. It has been generally accepted that primary and secondary amyloidosis can be distinguished. Amyloidosis of leprosy patients is thought to derive from immunologic responses to leprosy bacilli, to various complications in the kidney and other organs, to changes of reticuloendothelial system associated with chemotherapy, or to some other factors. Therefore, it seems too simple to classify amyloid deposition in leprosy patients as being secondary only because of its association with leprosy. Recent studies have revealed an important role of immunoglobulins, especially light chain, in amyloid pathogenesis [6, 7]. However, amyloidosis has also been observed in cases with agammaglobulinemia [18, 28]. Therefore, it would be more significant to regard systemic amyloidosis as amyloidosis with or without excess immunoglobulin synthesis than to follow the traditional classification into "primary" and "secondary" types.

A study by Hardt and Claësson [9] indicated existence of amyloid-inducing factor released from dying thymus-dependent lymphoid cells. Franklin and Zucker-Franklin [6] presented a simplified pathogenic mechanism for amyloidosis as being the excessive antigenic stimuli to the immune system or the escape from normal immune control mechanism. Amyloid deposits associated with leprosy seem to be worth more strict immunologic reexamination, clinically and pathologically, though leprosy has been simply understood as one of the chronic infectious stimulations to amyloid pathogenesis.

Foreign body type giant cells were observed in the severely amyloid kidney of a case in Group A (KK57-15). Several studies of experimental amyloidosis report the presence of foreign body giant cells and macrophages around the amyloid deposits in the spleen [22, 29] or in the liver and spleen [15], suggesting a resorptive process. Symmers [27] reported the presence of foreign body giant cells and macrophages around amyloid deposits of the spleen and lymph nodes. James [12] observed foci of foreign body cells and epithelioid cells in a case of amyloid goiter. The case reported by Lowenstein and Gallo [16] showed no resorption of mesangial amyloid deposits after remission of the nephrotic syndrome in renal amyloidosis, following treatment of original infectious diseases. As far as we know, there is no report of giant cell formation in human renal amyloid lesions as found in case KK57-15 in Group A. The findings of this case suggest the possibility of resorptive process in human renal amyloidosis, though its effectiveness is suspect.

## SUMMARY

Histopathologic studies were performed on systemic amyloidosis of leprosy patients in two Japanese leprosaria. Amyloid deposits were observed in 23 of 50 cases (46%) autopsied from 1955 to 1959 (Group A), and in 17 of 110 cases (15.4%) from 1962 to 1971 (Group B). These incidences are higher than those of the pre-chemotherapeutic period in Japan. The average age of amyloidal cases was significantly lower than that of nonamyloidal cases in both groups. There was no predilection for either type of leprosy in Group B. Pyelonephritis was frequently observed in both groups; the incidence of amyloidosis in Group B correlated with pyelonephritis. Amyloid deposits may be related to renal disorders associated with lepra reactions or inflammatory lesions. Amyloidosis has been classified into primary and secondary type, but the criteria seem uncertain. We referred to a classification based on immunologic findings. In the severely affected lesion of the kidney of one case, we observed foci of foreign body type giant cells, suggesting a possibility of resorptive process in human renal amyloidosis.

## RESUMEN

Se realizaron estudios histopatológicos de amiloidosis sistémica de los pacientes con lepra en dos leprosarios de Japón. Se observaron depósitos de amiloide en 23 de 50 casos (46%) autopsiados entre 1955 y 1959 (Grupo A), y en 17 de 110 casos (15.4%) desde 1962 a 1971 (Grupo B). Estas incidencias son más altas que las que se encontraban en Japón durante el período prequimioterápico. La edad promedio de los casos con amiloidosis fué significativamente menor que la de los casos negativos en ambos grupos. En el grupo B no hubo predilección por ninguno de los tipos de lepra. En ambos grupos se observó pielonefritis con frecuencia; la incidencia de amiloidosis en el Grupo B está relacionada con la de la pielonefritis. Los depósitos de amiloide pueden relacionarse a desórdenes renales asociados con reacción leprosa o lesiones inflamatorias. La amiloidosis se ha clasificado en primaria y secundaria, pero los criterios no parecen muy exactos. Nosotros nos referimos a una clasificación basada en hallazgos immunológicos. En un caso, en el cúal hubo lesión grave de un riñón, observamos focos de células gigantes tipo cuerpo extraño, sugiriendo la posibilidad de un proceso de reabsorción en la amiloidosis renal humana.

## RÉSUMÉ

Des études histo-pathologiques ont été menées concernant l'amyloïdose systémique, chez des malades de la lèpre de deux léproseries japonaises. Parmi 50 cas autopsiés de 1955 à 1959 (Groupe A), 23 soit 46%, ont révélé des dépôts amyloïdiques; de 1962 à 1971 (Groupe B), le nombre de tels cas s'est élevé à 17 sur 110, soit 15,4%. Ces incidences sont plus élevées que celles qui ont été observées au Japon durant la période ayant précédé la chimiothérapie. L'âge moyen des cas d'amyloïdose était significativement plus bas que celui des cas sans amyloïdose, et ceci dans les deux groupes. Dans le Groupe B, on n'a noté aucune prédilection pour l'un ou l'autre type de lèpre. Dans les deux groupes, on a fréquemment observé une pyélonéphrite; l'incidence d'amyloïdose dans le Groupe B montrait une corrélation avec la pyélonéphrite. Les dépôts d'amyloïde peuvent être mis en relation avec des désordres rénaux associés avec la réaction lépreuse ou avec des lésions inflammatoires. L'amyloïdose a été classée en type primaire et en type secondaire, mais les critères semblent incertains. Les auteurs se sont référés à une classification basée sur les observations immunologiques. Dans un cas de lésion grave du rein, on a observé les foyers de corps étrangers du type de cellules géantes, ce qui suggère la possibilité d'un processus de résorption dans l'amyloïdose rénale humaine.


**Acknowledgments.** We wish to acknowledge with gratitude the histologic preparations of Mr. S. Matsumoto, chief technologist of Oku Komyoen. Our thanks are also due to Mr. S. Mizo, Mr. M. Koike, and Mr. Y. Funamoto for their technical and photographic assistance.

## REFERENCES


1. Azzopardi, J. G. and Lehner, T. Systemic amyloidosis and malignant disease. J. Clin. Pathol. **19** (1966) 539-548.
2. Brownstein, M. H. and Helwig, E. B. Secondary systemic amyloidosis: analysis of underlying disorders. South. Med. J. **64** (1971) 491-496.
3. Contreras, Jr., F., Terencio de las Aguas, J. and Contreras, F. Hepatic lesions in lepromatous patients. Int. J. Lepr. **37** (1969) 270-279.
4. Desikan, K. V. and Job, C. K. A review of postmortem findings in 37 cases of leprosy. Int. J. Lepr. **36** (1968) 32-44.
5. Eliakim, M. and Rosenmann, E. Renal amyloidosis in a patient with recurrent polyserositis previously manifesting proteinuria with minimal glomerular changes. Isr. J. Med. Sci. **8** (1972) 53-56.
6. Franklin, E. and Zucker-Franklin, D. Current concepts of amyloid. *In:* Advances in Immunology. F. J. Dixon and H. G. Kunkel, eds., New York and London: Academic Press, vol. 15, 1972, pp 249-304.

7. GLENNER, G. G. The discovery of the immunoglobulin origin of amyloid fibrils and its pathogenetic significance. Acta Pathol. Microbiol. Scand. (A) **80**, Suppl. 233 (1972) 114-121.
8. HARDT, F. Acceleration of casein-induced amyloidosis in mice by immunosuppresive agents. Acta Pathol. Microbiol. Scand. (A) **79** (1971) 61-64.
9. HARDT, F. and CLAËSSON, M. H. Quantitative studies on the T cell populations in spleens from amyloidotic and nonamyloidotic mice. Immunology **22** (1972) 677-683.
10. HELLER, H., MISSMAHL, H. P., SOHAR, E. and GAFNI, J. Amyloidosis: its differentiation into peri-reticular and peri-collagen types. J. Pathol. **88** (1964) 15-34.
11. INABA, T. Systemic amyloid degeneration in autopsy cases of leprosy. Lepro **14** (1943) 508-513. (In Japanese)
12. JAMES, P. D. Amyloid goitre. J. Clin. Pathol. **25** (1972) 683-688.
13. KRISHNAMURTHY, S. and JOB, C. K. Secondary amyloidosis in leprosy. Int. J. Lepr. **34** (1966) 155-158.
14. LENDRUM, A. C., SLIDDERS, W. and FRASER, S. Renal hyalin. A study of amyloidosis and diabetic fibrinous vacuolosis with new staining method. J. Clin. Pathol. **25** (1972) 373-396.
15. LEVINE, S. and HOENIG, E. M. Amyloidosis in parabiotic gerbils. Arch. Pathol. **94** (1972) 461-465.
16. LOWENSTEIN, J. and GALLO, G. Remission of the nephrotic syndrome in renal amyloidosis. N. Engl. J. Med. **282** (1970) 128-132.
17. LÜDERS, K. Amyloidoseerwartung und Grundkrankheit. Klin. Wochenschr. **49** (1971) 570-574.
18. MAWAS, C., SORS, C. and BERNIER, J. J. Amyloidosis associated with primary agammaglobulinemia, severe diarrhea and familial hypogammaglobulinemia. Am. J. Med. **46** (1969) 624-634.
19. POLLIACK, A., LAUFER, A., GEORGE, R. and FIELDS, M. The effect of cortisone on the formation and resorption of experimental amyloid. Br. J. Exp. Pathol. **54** (1973) 6-12.
20. POWELL, C. S. and SWAN, L. L. Leprosy: pathologic changes observed in 50 consecutive necropsies. Am. J. Pathol. **31** (1955) 1131-1147.
21. RAVID, M., GAFNI, J., SOHAR, E. and MISSMAHL, H. P. Incidence and origin of non-systemic microdeposits of amyloid. J. Clin. Pathol. **20** (1967) 15-20.
22. RICHTER, G. W. The resorption of amyloid under experimental conditions. Am. J. Pathol. **30** (1954) 239-261.
23. RIDLEY, D. S. Reactions in leprosy. Lepr. Rev. **40** (1969) 77-81.
24. RIDLEY, D. S. and JOPLING, W. H. Classification of leprosy according to immunity. A five-group system. Int. J. Lepr. **34** (1966) 255-273.
25. SASAKI, N. and KAWATSU, K. Pathological study of secondary amyloidosis associated with leprosy. Annu. Rep. Natl. Inst. Lepr. Res. **17** (1972) 25-30. (In Japanese)
26. SCHUTTLEWORTH, J. S. and ROSS, SR. H. Secondary amyloidosis in leprosy. Ann. Intern. Med. **45** (1956) 23-38.
27. SYMMERS, W. ST. C. Amyloidosis. Five cases of primary generalized amyloidosis and some other unusual cases. J. Clin. Pathol. **9** (1956) 212-228.
28. TEILUM, G. Pathogenesis of amyloidosis. The two-phase cellular theory of local secretion. Acta Pathol. Microbiol. Scand. **61** (1964) 21-45.
29. WILLIAMS, G. Histological studies in resorption of experimental amyloid. J. Pathol. **94** (1967) 331-336.
30. WILLIAMS, JR., R. C., CATHCART, E. S., CALKINS, E., FITE, G. L., TUBIO, J. B. and COHEN, A. S. Secondary amyloidosis in lepromatous leprosy. Possible relationships of diet and environment. Ann. Intern. Med. **62** (1965) 1000-1007.
31. WRIGHT, J. R., CALKINS, E., BREEN, W. J., STOLTE, G. and SCHULTZ, R. Relationships of amyloid to aging. Review of the literature and systematic study of 83 patients derived from a general hospital population. Medicine **48** (1969) 39-60.