(6) Pathology of Amyloidosis

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Although various changes have been noticed in manifestation and/or incidence of many diseases, a remarkable increase of amyloidosis in Japan after the IInd World War may be one of the most unique trend in medicine.

The incidence of amyloidosis confirmed by autopsy in Japan from 1926 to 1967 (Showa-era) is plotted in Fig. 1. There were 242 autopsy cases of amyloidosis during the recent 10 years among a total of 139,613 autopsies with a ratio of 1.73%, which is nearly same as that of Italy reported in 1964. Subsequently, a further increase of this disease is to be expected in Japan.

A problem would have raised whether this rapid increase is due indeed to an actually increased incidence of the disease or referable to advanced diagnostic technics in recent years. We would think that the both factors should be considered

![Figure 1. Per 3 year's number of autopsy cases.](image-url)
for the increase and especially a change of dieting in the Japanese should also be accounted for it.

The 242 cases of amyloidosis included 94 cases (38.8%) of primary type with 4 of family type, 104 (43%) of secondary type, 35 (14.5%) of myeloma-associated type, 7 (2.8%) of localized type and 2 (0.8%) of unclassified.

Regarding background diseases for the secondary amyloidosis, tuberculosis and leprosy are found to be most frequent in incidence as they were so in previous reports. It is, however, noticeable that malignant neoplasms other than multiple myeloma were the background in approximately 17% of the secondary cases and rheumatism in approximately 5%.

Age incidence of the primary amyloidosis distributed in a wide range from the 1st to 8th decades with peak incidence in the 5th to 6th decades as previously reported. Sex incidence of the primary amyloidosis was found to be contrary to that of previous reports, namely, the male patient was 0.58% in incidence, while the female was 0.82%.

Age incidence of the secondary amyloidosis also distributed widely and there were patients younger than 10 years of age such as 3 or 9 years. The sex incidence indicated almost no difference.

Organ involvement by amyloidosis was proved to be different in frequency between the primary and secondary types in the present study. In the primary type, there were two groups according to the frequency of the organ involvement; the most predominant group in which the liver, heart, spleen and kidney were involved by the disease in approximately 90% of the cases and the other group in which the adrenal, G.I. tracts and pancreas were involved in approximately 70%. In the secondary type, no distinct grouping was discernible in frequency in which the involvement of the spleen (87.5%), kidney (78.6%), pancreas (62.5%), liver (56.7%), G.I. tracts (approx. 45%), adrenal (38.5%) and others appeared arbitrarily.

A number of new pathological findings were observed in the present cases with amyloidosis and some new interpretations were made on the findings ordinarily reported. The heart showed a frequent and peculiar fibrosis in its both ventricles. This cardiac fibrosis has been considered to be an ischemic scar by many researchers, but we rather interpret it as originating from an amyloid degeneration and disintegration of the myocardial cells. In the spleen, there was a frequent amyloid degeneration of trabeculae and/or capsules, and it is considered to be the degeneration of muscular elements of these structures. A similar degenerative change was noticed in pancreatic glandular epithelia. The kidney did not reveal a glomerular sclerosis referable to amyloidosis. The thyroid, which is one of the organs affected most frequently by amyloidosis, also disclosed an amyloid degeneration of muscle-like element in the stroma. The most prominent finding in the involved G.I. tracts was an amyloid degeneration in the muscularis mucosae, which was followed occasionally by the similar degeneration of the muscularis propriae in severe cases.
The bone marrow and lymph node, particularly the former, were affected rather infrequently and slightly by amyloidosis. The CNS revealed an amyloid degeneration within the wall of blood vessels only in the meninges in 7 out of 21 cases examined (33%). Capillaries, arteries and veins in various organs were involved by amyloidosis and the main site of the degeneration in the latter two appeared to be in smooth muscle elements included in their walls.

Thirteen years ago the author reported a possibility to determine how old a given amyloid substance was by checking the argentaffinity in PAM-stained specimens\textsuperscript{25}. Recently we made the criteria for determining the argentaffinity in specimens with various thicknesses and led to the conclusion that amyloidosis progresses over several months to several years.

In the other previous report\textsuperscript{3}, we established 3 structural types for amyloid substance by the use of polarization microscope, that is pre-amyloid, typical amyloid and post-amyloid. It is found in the present study that the pre-amyloid does not produce any birefringence, the typical amyloid produces green and/or yellow bire-
fringence and the post-amyloid does orange or even orange-red one. Furthermore, we found fine granular elements and "ring units" composing amyloid substance in addition to fibrillar elements by a high resolution electron microscopic investigation. These fine granular elements and ring units are assumed to be compatible with a pre-amyloid substance.

The Fig. 2 showing a thyroid tissue obtained by biopsy indicates an intracytoplasmic production or more probably secretion of the fine granular pre-amyloid as well as fibrillar amyloid. It is assumed that the amyloid secretion by various cells including smooth muscle cells and even epithelial cells is a kind of horocrine type. The opinion that amyloid can be produced only by reticulum cells seems not agreeable to us.

In regard to the etiology of amyloidosis, a complex of causality may have to be proposed.

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References