2. The Peripheral Neuropathies

2-(1) Correlation between Pathological Alterations and Functional Disorders in the Peripheral Neuropathies

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The pathological studies of the biopsied sural nerves were performed with special reference to which constitutional elements of the peripheral nerve would be primarily involved.

Materials and Methods:

The cases used for this study are listed in Table 1. The biopsied specimens were fixed in 10% formalin. A part was embedded in paraffin. The 5 μ sections stained with H. & E., Masson's trichrome and Bodian's methods were examined with light microscope. The teased fibers were isolated from another part of the fixed specimen and measured for the internodal lengths and fiber diameters. The electronmicroscopic study was made on several cases.

Table 1. Materials

Charcot-Marie-Tooth disease	4 Cases
Diabetic neuropathy	10
Myxedema neuropathy	4
Collagen disease	7
INH neuropathy	6
Ethambutol neuropathy	6
SMON	22
n-Hexane neuropathy	6
Control	15
Total	80

Results:

The sural nerves taken from clinically severe and/or chronic cases showed degeneration and disappearance of axons and myelin sheaths altogether in high grade. The Schwann cells and connective tissue were increased, as well as small blood vessels. The walls of blood vessels were frequently thickened and degenerated. Consequently, it was difficult in these severe and/or chronic cases to elucidate the mainly involved element in the peripheral nerves.

In the cases with relatively milder neurological symptoms, however, there was a tendency that a mainly involved site was different according to the etiology of neuropathies. The pathological changes of the sural nerves taken from the milder cases will be described below:

In Charcot-Marie-Tooth disease (CMT) and diabetic and myxedema neuropathies, the changes of the myelin sheaths were severer than those of axons. The great variety in internodal distance observed in the teased fibers seems to suggest segmental demyelination and/or regeneration.

The connective tissue of the peripheral nerves in CMT was moderately increased but not extraordinarily as seen in Déjerine-Sottas disease. The onion-bulb formation was not proved either in light or electron microscope.

In sural nerves of diabetic cases, many blood vessels showed degenerative changes and thickening in their walls. Some had occlusive changes.

In myxedema neuropathy, the homogeneous substance was observed in subperineurial space of the nerves. This showed metachromasia with toluidin blue and cresylviolet stains.

The grade of axonal damages was equal to or higher than the changes of myelin sheaths in the neuropathy associated with collagen disease and in INH, Ethambutol (EB), Clioquinol (SMON) and n-Hexane neuropathies. The teased fiber of these cases had a tendency to have uniformly short internodes irrespective of their diameters. This finding is considered to be due to Wallerian degeneration. Some fibers showed segmental demyelination mixed with Wallerian type degeneration.

The nerves from the cases of collagen disease showed inflammatory cell infiltration around the blood vessels and the thickening of blood vessels.

The pathological findings in various neuropathies are summarized in Table 2. The size of circle demonstrates the grade of pathological alteration. The arrow indicates that the blood vessel changes would influence the alterations of nerve fibers in diabetes mellitus and collagen disease.

Table 2. Grade of pathological alteration

	Axon	Myelin sheath	Blood vessel
Charcot-Marie-Tooth disease	●	●	
Diabetic neuropathy	●	● ~ ●	◁ ●
Myxedema neuropathy	●	●	
Collagen disease	●	●	◁ ●
INH neuropathy	●	●	
EB neuropathy	●	●	
SMON	●	●	
n-Hexane neuropathy	●	●	

Discussions:

The cases studied in the present study could be grouped in two according to the comparison of grades of changes between myelin sheath and axon. The first group in which severer changes were observed in the myelin sheath included CMT and diabetic and myxedema neuropathies. The myelin sheath and Schwann cell which governed the former would be the primarily disturbed site. The second group in which axonal damages were higher than or equal to the myelin sheath changes included collagen disease and INH, EB, Clioquinol and n-Hexane neuropathies. The primarily involved element in the second group was considered to be

the axon and their mother cell, that is, the nerve cell in the spinal dorsal ganglion.

Dyck and Lambert (1968) tried to divide the cases of CMT in two types, Schwann cell type and neuronal type, from the pathological point of view. The former was considered to have the original disturbance in the Schwann cell and showed segmental demyelination and remyelination with hypertrophy of the peripheral nerves. The latter had the main problem in the nerve cells and showed segmental demyelination to a less extent. All our cases had segmental demyelination in high grade and frequent remyelination. So they would belong to the Schwann cell type. However, hypertrophy of the peripheral nerve was not observed.

The changes of the blood vessels in the nerves of diabetic patients were not enough to explain the broad demyelination. As Thomas and Lascelles (1966) and Chopra et al. (1969) mentioned, metabolic disturbance of diabetes mellitus itself would cause the disruption of the metabolism of Schwann cell and myelin sheath.

In myxedema neuropathy, the mechanical compression of the metachromatic substance to the nerve fiber would be a factor of demyelination seen in the sural nerve. Beside that, the existence of wider metabolic disorder would be suspected.

The disturbance of blood circulation was considered to play an important role in etiology of peripheral nerve lesions in collagen disease. In intoxication neuropathies such as INH, EB, Clioquinol and n-Hexane neuropathies, the metabolic disturbance in the peripheral nerve has not been known yet, except the fact that INH would block the process of phosphorylation of pyridoxine.

Summary:

Sixty-five biopsied sural nerves from various neuropathies were examined pathologically. Morphological characteristics of each neuropathies were described with special reference to the primarily damaged site in the nerves. Correlation between morphological alterations and functional disorders in various neuropathies was discussed.

References:

- 1) Chopra, J. S. et al.: Brain 92: 391, 1969.
- 2) Dyck, P. J. and Lambert, E. H.: Arch. Neurol. 18: 603, 1968.
- 3) Thomas, P. K. and Lascelles, R. G.: Quart. J. Med. 35: 489, 1966.