2-(2) Quantitative Studies on Sural Nerves in Patients with Peripheral Nerve Diseases and Control Subjects

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The purpose of the present report is to study quantitatively the changes of biopsied sural nerves in patients with peripheral nerve diseases in comparison with control subjects. The changes with age in control sural nerves were also determined quantitatively. Furthermore, animal experimentation was made in an attempt to evaluate the significance of some results obtained from human pathological materials. The results were as follows.

(1) Age changes of the densities of myelinated fibers and cell nuclei in control sural nerves:

Small myelinated fiber density was 26,300/mm² at the age of one week and decreased rapidly until the second decade (9,575/mm²) and then decreased more gradually with advancing age. Average small myelinated fiber density at the 8th decade (6,670/mm²) was 70% of that at the second decade.

Large myelinated fibers appeared first at the age of 5 months. Its density showed a steep increase up to approximately 3 years of age attaining the level of a young adult, became maximum at the third decade (6,480/mm²), and thereafter decreased with age. Average density at the 9th decade was 54% of that at the second decade. Therefore, the chronological decrease of the large myelinated fiber density was more marked than that of the small myelinated fiber density.

The nuclear population decreased from birth to the second decade and subsequently increased with age. Average population at the 8th decade reached 165% of that at the second decade.

(2) Changes of myelinated fiber density and cell nuclei in biopsied sural nerves of patients with peripheral nerve diseases:

Normality or abnormality of biopsied sural nerves of patients with peripheral nerve diseases should be estimated in comparison with control subjects. For this reason, the value (x) of myelinated fiber density or nuclear population in each pathological sample was standardized according to the formula; $z = (x - \bar{x})/s$, where $\bar{x}$ is average and s is standard deviation of the same age group, z being standard measure of x .

Fig. 1 shows frequency distribution of the standard measure of myelinated fiber density in controls and peripheral nerve diseases. In control materials, standard measure for both large and small myelinated fibers revealed roughly a Gaussian

Fig. 1. Frequency distribution for standard measure of myelinated fiber density.

distribution. In peripheral nerve diseases, the distribution curves were shifted to the left, thus implying a reduction of myelinated fiber density compared with control subjects. It should be noted that in cases of chronic polyneuritis and heredo-degenerative neuropathies, the decrease of large myelinated fibers was more marked than that of small myelinated fibers.

As for the nuclear population, less than 20% of control subjects as well as subjects with acute polyneuritis and SMON had their standard measure higher than +1, while 55% of chronic polyneuritis and 92% of heredo-degenerative neuropathies had their standard measure greater than +1.

(3) Changes of cellular proportion, number and diameter of unmyelinated fibers (Figs. 2 and 3):

Fig. 2. Changes of nuclear proportion.

Fig. 3. U.F.=Number of unmyelinated fibers.

Ochoa and Mair (*Acta neuropath.*, 13: 197, 217, 1969) showed a larger proportion of Schwann cells without axon in a man aged 59 than in a 15 year old boy. They also showed that the percentage of small unmyelinated fibers was increased with age, but that the unmyelinated fiber density remained unchanged. In comparison with their results observed in control materials, our patients with acute polyneuritis and SMON showed neither changes in cellular proportion nor unmyelinated fiber density, but revealed a moderate increase in percentage of small unmyelinated fibers of less than 0.5μ in diameter. Chronic polyneuritis could be divided into two groups, A and B, according to the difference in the mode of changes of cellular proportion and unmyelinated fiber density (Figs. 2 and 3). Chronic polyneuritis-A revealed an increase of Schwann cells devoid of axon, while chronic polyneuritis-B an increase of Schwann cells containing unmyelinated fibers. In both groups, the percentage of small unmyelinated fibers (suggesting regenerating unmyelinated axons) to total unmyelinated fibers was remarkably increased. The unmyelinated fiber density was increased only in chronic polyneuritis-B. Therefore, the changes in the numbers of nuclei and cellular proportion were closely related to alterations in the number- and size-frequency histogram of unmyelinated fibers.

(4) Experimental Wallerian degeneration and chionoform neuropathy in animals:

It was confirmed in experimental animals that there was a close relationship between the quantitative changes of Schwann cells and those of unmyelinated fibers. Chionoform neuropathy without remarkable changes in unmyelinated fibers showed no changes in either nuclear population or cellular proportion. In Wallerian degeneration with extensive damage and disappearance of unmyelinated fibers, there was a remarkable increase in nuclear population, especially nuclei of Schwann cells devoid of axon.

In conclusion, it was emphasized that as control sural nerves revealed remarkable chronological changes, any results in pathological materials should necessarily be compared with control materials of the same age group. It was also pointed out that since Schwann cells containing unmyelinated axons constituted most of the cells inside the perineurium, quantitative changes of cell nuclei depended largely upon alterations of unmyelinated fibers.