CHANGES IN THE PERIPHERAL NERVOUS SYSTEM DUE TO EXPERIMENTAL FEVER

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Studying the condition of the peripheral nervous system during certain diseases, B. I. Lavrentyev and his colleagues [13, 14] found a series of changes in the nerve fibers and in their endings which were not characteristic of Wallerian degeneration. They were mainly expressed in the disturbance of the ability to adsorb silver salts, in surplus growth and in the formation of varicosities, which sometimes were like coarse thickenings deforming the fiber. The earliest changes, which are reversible, B. I. Lavrentyev treated as "symptoms of irritation". Such an affection of the nerve apparatuses, prior to change in the innervated tissue, he considered to be the morphological equivalent of disfunction of the nerve fiber and synapse.

The studies of many authors have shown that reaction changes of the peripheral nerve apparatuses are observed in the most diverse diseases, when, as under experimental conditions, they are first detected in the afferent part of the peripheral nervous system.

The purpose of our study was to investigate the presence and character of morphological changes in certain elements of the peripheral nervous system under fever conditions.

The works of P. N. Veselkin [1-3] and his colleagues have established the importance of the nerve mechanisms, and that of the peripheral neuro-receptoral apparatuses in particular, to the realization of a fever reaction.

B. A. Dolgo-Saburov [4, 5, 6, 7] and V. V. Kupriyanov [10, 11] have shown the high reactivity of the receptoral apparatuses in the wall of the caval veins and vessels of the lesser circulatory system during different pathological conditions (de-efferentation, oxygen deficiency, uremia, anemia, etc.). We conducted our studies on these same vessels and on the portal vein. Besides the receptor fibers and their endings, we also studied the nerve trunks (vagus nerves) and the cell bodies of the neurons which provide sensory innervation of the indicated veins, i. e., we studied the nodose ganglia of the vagus nerves and the intervertebral ganglia of the corresponding segments of the spinal cord.

EXPERIMENTAL METHODS

Cats were used as the experimental animals. The fever reaction was caused by a subcutaneous hip injection of a Bacillus mesentericus culture. In one series of experiments, 2 ml of a pyrogenic culture to each kilogram of the animal's weight (optimal dose) was injected, in the other – 8 ml for increased irritation.

The experiments were done on 50 cats in series of five animals each. The cats were kept in identical conditions for 2-3 days, then three of them were injected with the pyrogenic irritant, and the two control animals were injected with the same amount of a physiological solution.

The temperatures – the original and that after the irritant injection – showed a fever reaction in all of the animals. The maximal temperature increase was 2°. The larger doses of the injected irritant caused the same temperature reaction.

The animals were killed by ether inhalation.

Material for morphological examination was taken after 1, 3, 4, 6-8, 15-18 and 24 hours, and also 6 days after the beginning of the experiment.

The items to be studied were histologically processed according to the methods of Bielschowsky–Gross, Ramon, Nissl and Marchi.

EXPERIMENTAL RESULTS

Examination of the walls of veins taken from the animals one hour after the pyrogenic irritant injection showed no change in the condition of the peripheral nerve apparatuses.

A study of preparations obtained 3-4 hours after the culture injection, i. e., the beginning of the increased temperature period (in the injections of both the optimal and larger doses of the pyrogenic irritant), showed that reaction changes were present in the nerve apparatuses in the caval and pulmonary vein walls. The same was noted on preparations obtained 5-8 hours after the culture injection, i. e., the period of maximal temperature rise.

Along with a heightened affinity to silver (argentophilia), considerable thickening of the myelinated nerve fibers was noticed, mainly in their preterminal sections. Some of the swollen, deformed fibers ended in a dense terminal branching (Fig. 1). In others, we also noticed a marked coarsening and thickening of the actual endings, the branches of which were greatly impregnated and looked like large bulbs. In the vein walls of animals killed 3-4 hours after the injection, we often found such nerve fibers which terminated in a blunt, "stump-like" end among a mass of special cells forming a "sensory bed" (Fig. 2).

Secondary Wallerian- type degeneration of the fibers was, as a rule, not observed. Unchanged nerve endings appeared relatively rarely on the preparations obtained 3-4 hours after the culture injection. There were no deviations from normal structure in the nervous apparatuses of the portal vein wall.

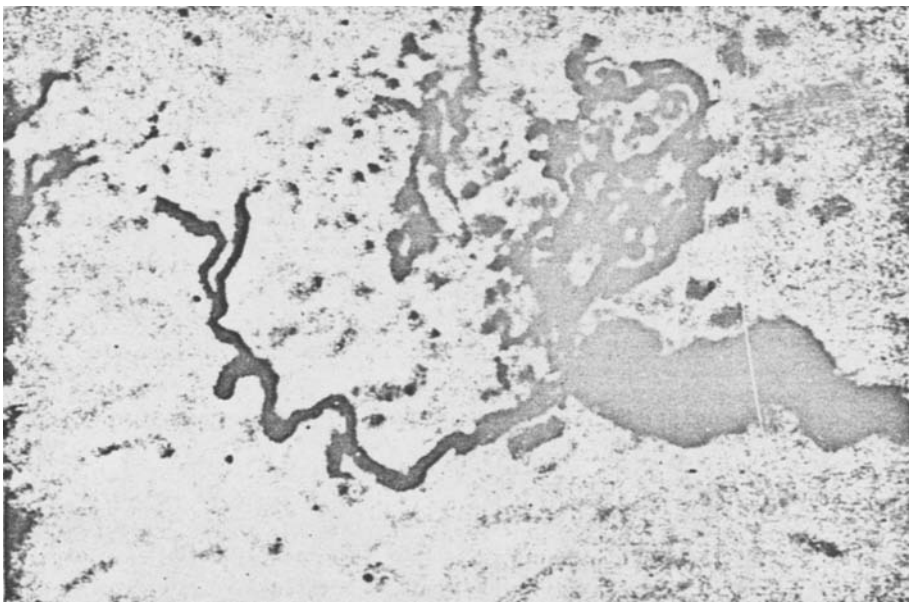

Fig. 1. Coarse thickening in the preterminal section of a receptor fiber in the wall of the superior vena cava of a cat.

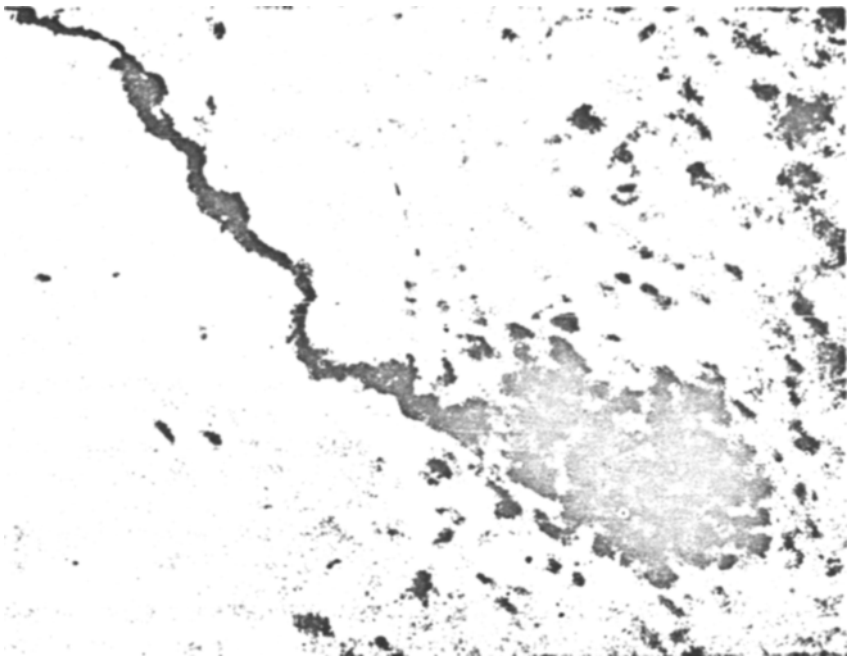

Fig. 2. "Stump" of a nerve fiber, surrounded by a mass of special cells in the wall of the pulmonary vein of a cat.

Different results were obtained from studying vein preparations made from animals killed at later intervals after the pyrogenic substance injection. 15-18 hours after the start of the experiment, i. e., during the post-fever period, a larger number of normal sensory fibers and their endings was observed, and changed nerve apparatuses were found much less frequently. Among these, appeared receptors in the form of thin, frequently palely-impregnated, sparse branchings coming off the end or side of the fiber (Fig. 3). Sometimes similar branchings sprouted directly from the spherical thickening of the preterminal section of the fiber.

Fig. 3. Thin, delicate branchings on the end and side of a myelinated fiber in the wall of the superior vena cava of a cat.

Studying the vein preparations obtained still later after the start of the experiment – after 24 hours, in general, we did not find essential differences in the structure of the peripheral nerve apparatuses of either the experimental or the control animals. The same results were obtained from examining vein preparations from cats which had lived 6 days after the one-time injection of the pyrogenic irritant.

Studying the veins which had been processed by the silver methods, we did not observe changes in the elements of their efferent innervation in any of the experiments. The thin, nonmyelinated fibers of the vegetative nervous system were evenly impregnated, their contours uniform and smooth. The ganglionic nerve cells in the vein wall were normal; sometimes pericellular apparatuses were clearly evident on them.

These observations confirm the long-established opinion that the reactivity of the sensory innervation circuits is greater than that of the motor.

In order to examine the condition of the bodies of the sensory neurons, whose dendrites form the wall receptors of the vessels studied, we examined the nodose ganglia of the vagus nerves and the spinal ganglia of the upper and middle thoracic segments of the spinal cord, which are the sensory innervation sources of the caval and pulmonary veins. We noted only single cells with symptoms of primary irritation according to Nissl, or, more rarely, with serious changes. By computation, it was established that the number of such cells in the preparations from the experimental and control animals was approximately the same. No changes were found on longitudinal and lateral sections of the vagus trunks which were processed according to the Marchi method to determine the reaction of the afferent fibers.

The reaction changes that we did find in the receptor fibers and in their endings were all of the same type. It is true that some features of these changes were more usually found on material taken from animals at earlier intervals (the nerve fiber "stumps"), and that others were more often observed on preparations obtained from cats which had lived longer after the start of the experiment (the thin, pale terminal branches, which we believe to be a young form of receptor).

One can suggest that these and other features of the changes are the morphological expression of the different functional conditions of the neuron.

The nerve fiber "stumps" found on the histological preparations allow the proposal that autoreceptorotomy (similar to N. I. Zazybin's autoneurotomy) is possible as an adapting reaction of the neuron in response to the action of the injuring factor, with the subsequent regeneration of that neuron's dendrite and thus the restoration of the receptor. The great capacity of nerve fibers for growth and the considerable variability of the peripheral nerve apparatuses have been repeatedly mentioned by K. A. Lavrov [12] and by N. I. Zazybin [8, 9]. Regeneration of the receptors in the wall of the estuarial sections of the caval veins after their destruction, with a disturbance of the portal circulation, was observed by B. A. Dolgo-Saburov [7] in cats.

The character and sequence of development of the reaction changes give reason to suggest that they are morphological expressions of different functional conditions of the sensory neurons, as of the initial circuit of the analyzor mechanism, which first experiences the action of the foreign factor.

SUMMARY

Studies of the nervous apparatus of the large veins in animals with experimental fever caused by the injection of a culture of Bacillus mesentericus demonstrated reactive changes of the sensory apparatus in the walls of the superior vena cava and pulmonary veins with intact afferent innervation. Structural changes mainly in preterminal and terminal sections of the medullated fibers were as a rule detected in 3 hours after the injection of the stimulus, reached the maximum in 6-8 hours and disappeared in 24 hours. Neurons of the afferent innervation in walls of the g.nodosa and the spinal ganglions were not changed. The data obtained show that reactive changes caused by experimental fever first appear in the peripheral section of the neuron and are reversible.

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