CHANGES IN MOTOR AND SENSORY NERVE ENDINGS IN THE GASTROCNEMIUS MUSCLE DURING DEVELOPMENT OF AN INDUCED RHABDOMYOSARCOMA

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Investigations [8, 9, 10-13, 17] have shown that the development of a tumor is preceded by functional disturbances of the central nervous system. In these investigations, by the use of certain agents modifying the functional equilibrium of the central nervous sytem, changes were produced in the course of tumor development. Conversely, in morphological investigations changes have been found in the peripheral nervous system and also in the neurons of the spinal cord connected anatomically with the focus of tumor development [2, 5, 6]. During studies of various portions of the nervous system (in accordance with B. S. Doinikov's scheme) the initial changes in neurons belonging to afferent systems were demonstrated at levels corresponding to the innervation of the site of injection of the carcionogen in the course of tumor formation [9]. Subsequently, as these changes at the site of application of the carcinogen in the course of tumor formation [9]. Subsequently, as these changes at the site of application of the carcinogen increase, terminating in malignant growth, changes were observed in the motoneurons of the spinal cord and also in higher levels of the central nervous system.

The observations mentioned above, together with other data in the literature, indicate that the nervous system plays an important role in the pathogenetic mechanisms of tumor growth.

In the present investigation changes in the motor and sensory nerve endings in muscle tissue at the site of a focus of carcionogensis were studied.

EXPERIMENTAL METHOD

The investigation was conducted on male albino rats weighing 120-160 g, receiving an injection of 1 mg 9, 10-dimethyl-1,2-benzanthracene (DMBA), dissolved in 0.2 ml rat fat, into the same region. The animals were sacrificed after periods varying from 21 to 327 days inclusive. The right and left gastrocnemius muscles were investigated. The nerve endings were revealed by the Bielschowsky–Gros method as modified by Lavrent'ev, and by Campos's method. To identify changes at the site of injection of DMBA and BA, the material was stained by Van Gieson's method and with hematoxylin-eosin and Sudan III.

EXPERIMENTAL RESULTS

In early stages of the process (21st, 62nd, 90th days), when nonspecific inflammatory changes were present at the site of injection of DMBA around the periphery of cavities containing the carcinogen dissolved in fat (see figure, A), signs of irritation were seen in the motor endings of the left gastrocnemius muscle, in the form of thickening and coarsening of the preterminals and the terminal fibrils, together with an increase in the number of nuclei of the end-plate (see figure, B). In the neuromuscular spindles changes were observed in the nerve fibers, with signs of irritation (varices, pools of neuroplasm; see figure, C). On the 62nd day changes in the motor end-plates were found not only on the side of injection of DMBA but also in the opposite limb in the form of coarsening of the preterminal and terminal fibrils and the appearance of tiny spherical thickening at their ends (see figure, F).

With the onset of proleferative changes at the site of injection of DMBA (120th-150th day), besides signs of irritation (see figure, D) in the motor end-plates of the left gastrocnemius muscle, more severe changes were observed compared with those seen in the preceding stage of the process. Spherical swellings

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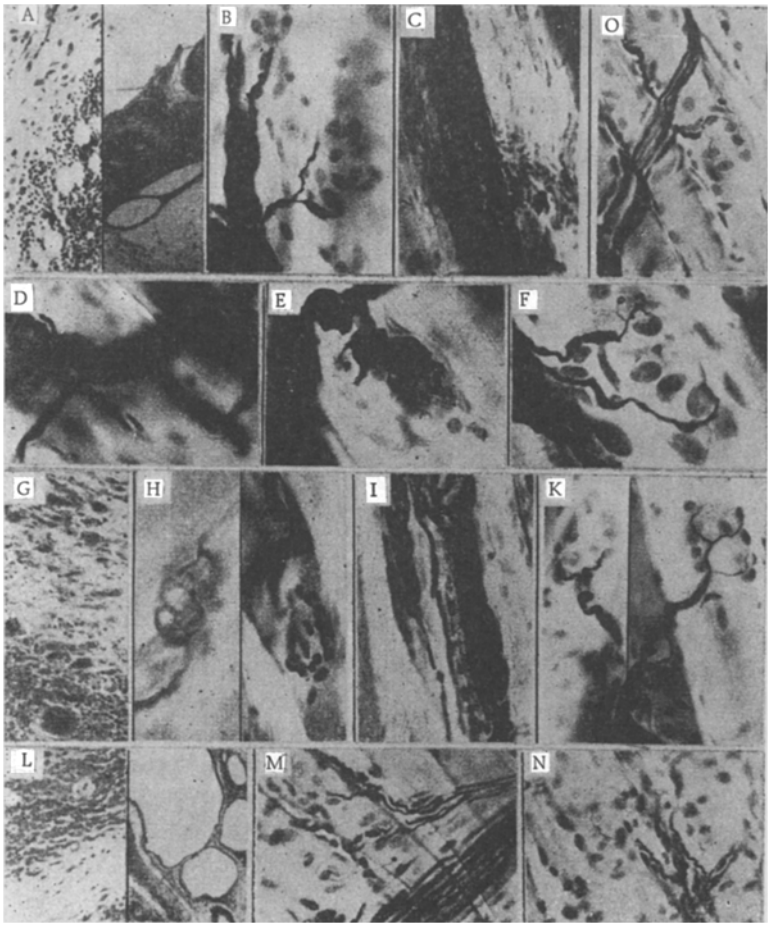

Changes in nerve endings in muscle during development of rhabdomyosarcoma. A) Left gastrocnemius muscle, 21st day after injection of carcinogen. Inflammatory reaction around cavities containing DMBA dissolved in fat. 10 × 20; B) motor end-plate of left gastrocnemius muscle of 21st day. Coarsening of preterminals, increase in number of nuclei in end-plate. 10 × 40; C) neuromuscular spindle of left gastrocnemius muscle on 21st day. Varices, pools of neuroplasm in nerve fibers. 10 × 40; D) motor end-plate of left gastrocnemius muscle on 120th day. Coarsening of preterminal and terminal fibrils. 10 × 40; E) motor end-plate of left gastrocnemius muscle on 150th day. Neuroma of endings. 10 × 90; F) motor end-plate of right gastrocnemius muscle on 62nd day. Coarsening of preterminal and terminal fibrils with formation of spherical thickenings on ends. 10 × 90; G) rhabdomyosarcoma, 327th day after injection of DMBA. 10 × 20; H) two motor end-plates of left gastrocnemius muscle on 327th day. End-plate whose terminal fibrils form a coarse argyrophilic glomerulus, and end-plate without terminal fibrils. 10 × 40; I) neuromuscular spindle of left gastrocnemius muscle on 327th day. Nerve fibers with varices and pools of neuroplasm. 10 × 40; K) motor end-plates of left gastrocnemius muscle with signs of irritation of preterminal and terminal fibrils and end-plate without terminal fibrils. 10 × 40; L) left gastrocnemius muscle. Inflammatory reaction around cavities with BA dissolved in fat. 10 × 40; M, N) motor end-plates of left gastrocnemius muscle on 21st day after injection of BA. Corkscrew-like twisting and intensified growth of terminal fibrils and formation of spherical thickenings of their ends. 10 × 40; O) motor end-plate of normal left gastrocnemius muscle. 10 × 40.

of considerable size (neuromas of the nerve endings; see figure, E) appeared at the ends of the terminal fibrils. Signs of irritation persisted in the motor end-plates of the controlateral limb.

With the appearance of a tumor of rhabdomyosarcoma type (210th-327th day; see figure, G) in the left gastrocnemius muscle, besides motor end-plates with signs of irritation of varying degree there were others in which the terminal fibrils had joined together to form coarse argyrophilic glomeruli. In other end-plates no terminal fibrils could be seen (see figure, H).

In the sensory neuromuscular spindles, as in the preceding stages, signs of irritation of their nerve fibers were present (see figure, I). The pattern of irritation of the preterminal fibrils was preserved in the motor end-plates of the contralateral limb, and terminal fibrils could not be detected in every case (see figure, K).

In the control animals inflammatory changes developed at the site of injection of BA in the early stages around the cavities containing BA dissolved in fat (see figure, L), but by the 150th day these had disappeared and were replaced by fully formed scar tissue. In the motor end-plates of the left gastrocnemius muscle in the early periods slight signs of irritation were observed, in the form of increased growth of the terminal fibrils and the formation of spherical thickenings on their ends (see figure, M and N), but later these were no longer found. No changes were present in the motor end-plates of the contralateral limb.

Hence, injection of a carcinogen (DMBA) into the left gastrocnemius muscle and the subsequent development of changes at the site of its injection are accompanied by injury to both motor and sensory nerve endings. These changes initially take the form of coarsening of the preterminal and terminal fibrils of the motor end-plates and an increase in the number of nuclei in the end-plate, and also of the appearance of varices on the axons of the neuromuscular spindles. Later, with progressive development of the proliferative changes and, in particular, with the appearance of malignant changes at the site of injection of the DMBA, the changes in the motor end-plates became more severe and destructive in character. The changes found in the sensory neuromuscular spindles throughout the experiment were of the character of irritation phenomena. Similar changes in peripheral nerve endings in skeletal muscles have been described by several investigators in experimental circulatory disturbances, in cases of spontaneous gangrene, and in other pathological conditions [1, 3, 19, 20].

Besides changes in the nerve endings on the side of injection of the carcinogen, changes were also found in the motor endings in the gastrocnemius muscle of the opposite limb starting with the 62nd day. However, the changes in the motor endings on the contralateral side were not so severe or destructive as those in the left gastrocnemius muscle.

Investigations by A. D. Speranskii's collaborators [4, 14-16, 18] showed that prolonged, chronic stimulation or division of a peripheral nerve fiber are accompanied by injury to the nerve endings not only on the side of the injured nerve, but also on the contralateral side, indicating segmental spread of disturbances in the nervous system. The changes found in the present investigations in the nerve endings of the contralateral limb following injection of a carcinogen into the left gastrocnemius muscle may also be evidence that in the case of growth of tumors the disturbances in the nervous system spread segmentally just as during development of degeneration in a nerve.

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