MORPHOLOGICAL CHANGES IN THE SPINAL GANGLIA AND SPINAL CORD OF RABBITS DURING DEVELOPMENT OF SHOPE'S VIRUS PAPILLOMA

A. E. Nadareishvili

Laboratory of Experimental Oncology of the Institute of Experimental Pathology and Therapy (Director, B. A. Lapin) and the Laboratory of Neurohistology (Head, Doctor Biol. Sci. E. K. Plechkova) of the Institute of Normal and Pathological Physiology (Director, Active Member AMN SSSR V. N. Chernigovskii) of the AMN SSSR, Moscow

(Presented by Active Member AMN SSSR V. N. Chernigovskii)

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During recent years many facts have been gathered showing that during the development of a tumor morphological changes are observed in the nerve cells, not only in the tumor itself and the surrounding tissues, but also in remote divisions of the nervous system (the spinal ganglia, the spinal cord and the brain) [1, 2, 4, 6, 7].

Since the role of viruses in the etiology of malignant neoplasms has received increasing attention, it was considered to be of interest to investigate the morphological picture of remote divisions of the central nervous system during the development of virus papilloma in rabbits.

EXPERIMENTAL METHOD

The material investigated consisted of the lumbar division of the spinal cord with the spinal ganglia corresponding to the segments of localization of the tumor (L3-L6) and, for purposes of comparison, from the same rabbits the cervical division of the spinal cord and the spinal ganglia (C6-C7). We examined the spinal cord and ganglia 7, 8 and 16 months after inoculation of the virus. The morphological changes in the spinal cord and ganglia were thus studied at a period before malignant transformation, and at a much later stage of development of the malignant tumor. Malignant change usually takes

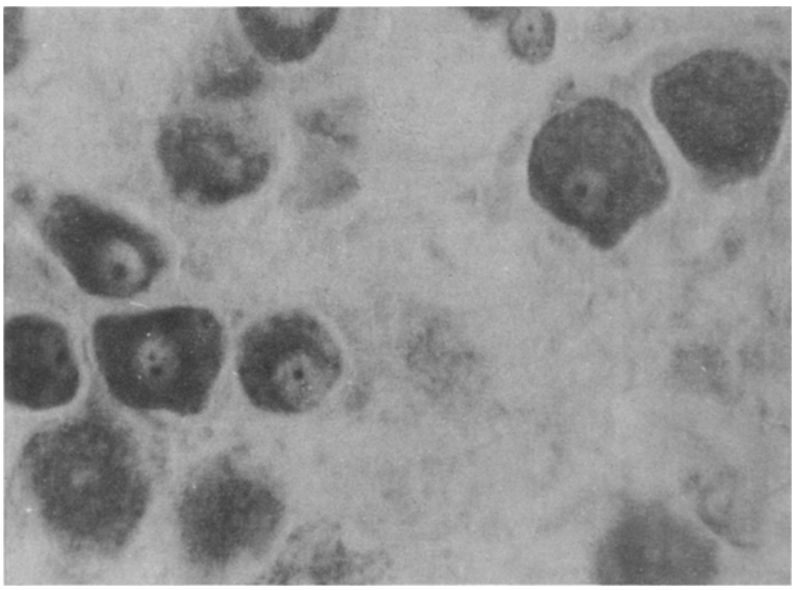

Fig. 1. Peripheral situation of the nucleus in nerve cells. Lumbar spinal ganglion; 7 months after inoculation with virus. Stained by Nissl's method. Objective 32×, ocular 6×, coefficient 1.9.

place in the papilloma at the 10th-12th month. The experiments were carried out on 8 rabbits. The sections were stained by Nissl's method.

EXPERIMENTAL RESULTS

Investigation of the spinal ganglia 7 months after inoculation with papilloma virus showed no abnormality of the overwhelming majority of nerve cells. Among them were nerve cells with a peripherally situated nucleus (Fig. 1) and individual nerve cells with perinuclear aggregation of the Nissl's granules. Occasionally large nerve cells could be seen with an uneven distribution of the Nissl's substance. In certain sections glial cells could be observed in close proximity to the body of the neurones, forming an impression on the surface of the neurones. Sometimes the pericellular spaces were widened. At the periphery of the ganglion in some sections hydropic cells were found with their nucleus displaced to the periphery of the body (Fig. 2). Capsules were seen in which only the remains of a neurone and collections of glial cells were present. In individual fields of vision the formation of glial nodules was observed at the site of dying nerve cells.

During investigation of the lumbar region of the spinal cord at the same period after inoculation, no abnormality was found in the majority of its cells. In individual sections, however, in the intermediate region and the posterior horns, nerve cells were found with a highly eccentric nucleus. Covering of nerve cells with glial elements was also observed. Meanwhile, in this region of the spinal cord, individual cells were found with rarefaction of the Nissl's substance at the periphery, and enlargement of the remaining Nissl's granules.

Whereas the above-mentioned changes were observed in the lumbar division of the spinal cord, no pathological changes affecting the nerve cells or glia were found in the cervical division of the spinal cord.

Eight months after inoculation with the virus, nerve cells with a peripherally situated nucleus were seen in the lumbar spinal ganglia, and in individual cells an ill-defined peripheral chromatolysis was observed. Occasionally the pericellular spaces were widened, and solitary hydropic nerve cells were observed.

At the same time, in these segments of the spinal cord, nerve cells with a peripherally situated nucleus and chromatolysis were rarely found. We never observed any pathological changes in the nerve cells in the cervical division of the spinal cord in this case.

Sixteen months after inoculation with virus the spinal ganglia showed changes analogous to those observed at the earlier periods, namely: nerve cells with the nucleus displaced to the periphery, and occasionally with peripheral chromatolysis and perinuclear distribution of the Nissl's substance. Along with these could be seen nerve cells with a perinuclear disposition of the Nissl's substance and an eccentrically situated nucleus, hyperchromatosis of the Nissl's substance and also sharply hyperchromatic hydropic nerve cells with the nucleus displaced to the periphery of the cell body. In individual sections proliferation of the glia was observed, with the formation of glial nodules or islets. As in the earlier periods, the changes described were found only in a proportion of the nerve cells.

Sixteen months after inoculation, more pronounced changes were found in the spinal cord than at the earlier periods. In the nerve cells with a peripherally situat-

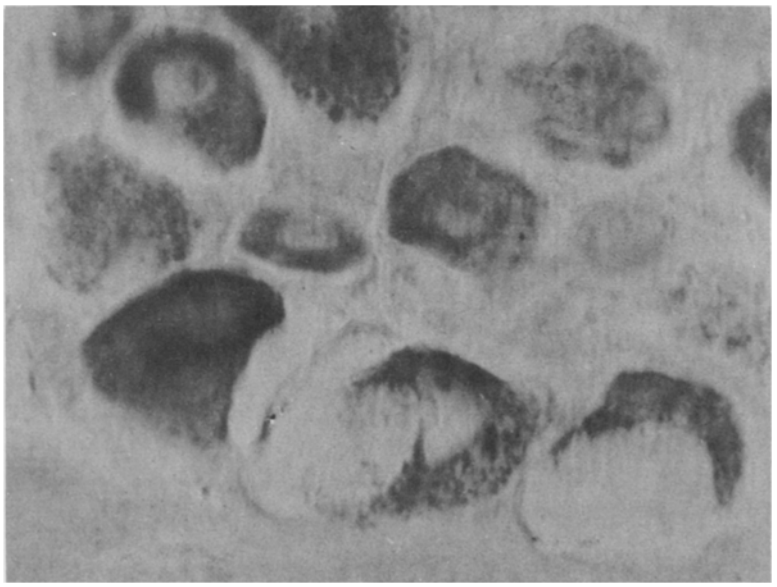

Fig. 2. Hydropic nerve cells. Lumbar spinal ganglion; 7 months after inoculation with virus. Stained by Nissl's method. Objective 50×, ocular 16×, coefficient 1.9.

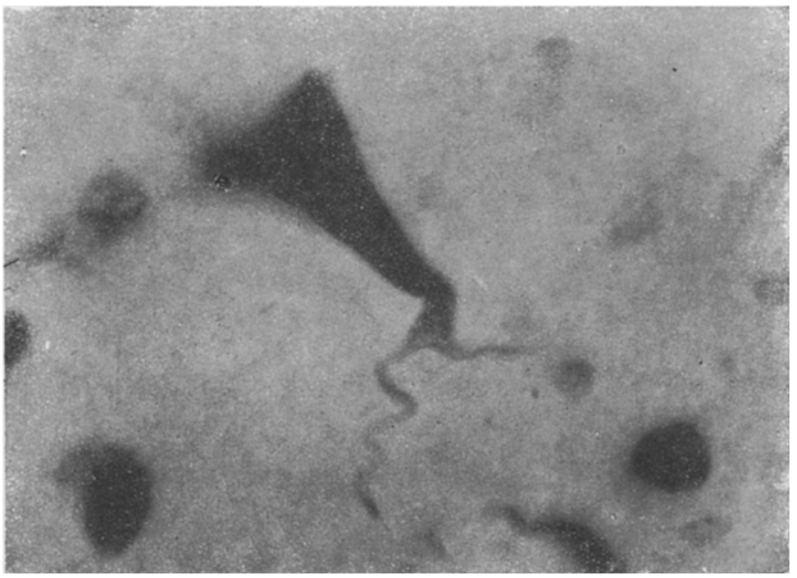

Fig. 3. Corkscrewlike twisting of the process of a nerve cell. Lumbar division of the spinal cord; 16 months after inoculation with virus. Stained by Nissl's method. Objective 95×, ocular 6×, coefficient 1.9.

ed nucleus and a Nissl's substance composed of large granules, a greatly enlarged nucleolus was observed, staining a dark color. In individual sections shrunken nerve cells could be seen along with chromatolysis. In the large neurones of the anterior and posterior horns, hyperchromatosis was observed, and their processes, twisted corkscrew-fashion, could be followed a long way (Fig. 3).

In the cervical division of the spinal cord in these rabbits, solitary nerve cells were found with an unevenly distributed Nissl's substance.

The results of the histological analysis may be summarized as follows: 7–8 months after inoculation with virus, signs of irritation of the nerve cells were observed in the spinal ganglia of the lumbar region of the spinal cord corresponding to the localization of the tumor. These took the form of the presence of nerve cells with a peripherally situated nucleus, an uneven distribution of the Nissl's substance, and so on. At the same time, nerve cells with more severe pathological changes were observed in the spinal ganglia, from which it could be judged that at this period after inoculation with virus, more severe, irreversible, destructive changes also took place. Evidence of this was the presence of hydropic cells, the formation of glial nodules at the site of death of the cells, and so on. So far as the spinal cord is concerned, only changes indicating irritation of the nerve cells took place. In the cervical division we found no pathological changes at this period after inoculation with the virus.

With the development of the tumor, the changes in the nerve cells of the spinal cord progressed. Sixteen months after inoculation with virus, profound pathological changes were observed in the nerve cells, not only of the spinal ganglia, but also in the spinal cord. In the lumbar division of the spinal cord, for instance, shrunken nerve cells with twisted, corkscrewlike processes appeared, giving evidence of more serious pathological changes. At this stage of development of the tumor, moreover, reactive changes were also observed in the cervical division of the spinal cord.

SUMMARY

The experiments thus showed that, in addition to the changes in the peripheral nervous system, previously studied by us in the tumor itself and in the surrounding connective-tissue capsule, changes also took place in the spinal ganglia and the spinal cord.

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