MORPHOPHYSIOLOGICAL ANALYSIS OF THE CHANGES IN THE SKIN AFTER INTERRUPTION OF ITS SYMPATHETIC INNERVATION

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Division of the sympathetic nerves is a method used to treat certain diseases (endarteritis obliterans, Raynaud's disease, etc.) [7, 12]. At the present time, however, no adequate answer has yet been given to the question of whether desympathization is a harmless procedure. Morphological investigation may make an important contribution to the solution of this problem.

The researches of physiologists (an exhaustive survey of the literature is given in the monograph by T. A. Grigor'eva [1]) have established that the sympathetic nervous system provides the motor innervation of the blood vessel wall. Exclusion of the sympathetic nerves prevents the normal vascular reactions from taking place. Recent physiological findings [6, 10, 11, 14] have confirmed this fact. It has also been shown that the efferent innervation of the arrectores pilorum muscles and of the sweat glands is provided by the sympathetic nervous system [8, 9].

T. A. Grigor'eva concludes from results obtained in her laboratory [2-4] that the smooth muscle and the autonomic motor which innervates it form an indissoluble functional and structural entity. In her opinion, exclusion of the sympathetic motor innervation of smooth muscle inevitably leads to its death by atrophy.

The object of the present investigation was to examine the morphological changes taking place in the skin immediately after sympathectomy.

EXPERIMENTAL METHOD

Experiments were conducted on 16 adult cats. The sympathetic innervation of the skin of the ear was interrupted by removal of the superior cervical sympathetic ganglia bilaterally or unilaterally. At intervals of between 2 days and 6 months after the operation the animals were sacrificed and pieces of skin were fixed in a 12% solution of neutral formalin and stained with hematoxylin-eosin, azure-II-eosin, or impregnated with silver by Kampos's method. The skin temperature was measured before the experiment, during sympathectomy, and at various intervals after the operation by means of an electrothermometer. At various intervals (from 10 min to 2 months) after sympathectomy the action of ether anesthesia on the blood vessels of the desympathized ear was studied by measurement of the skin temperature. The skin temperature of the intact ear of the same animal served as a control.

EXPERIMENTAL RESULTS

Neurohistological investigation showed that 48 h after the operation the sympathetic nerves were undergoing degeneration. Degeneration of the sympathetic nerve fibers was observed near the smooth muscles of the skin, mainly along the course of the blood vessels possessing a muscular coat. The sensory nervous apparatus of the desympathized skin remained intact. As was expected, the morphological changes were first seen in the skin structures incorporating smooth muscle (blood vessels, arrectores pilorum muscles, glands). At all periods after sympathectomy marked dilatation of the blood vessels was observed, and they were engorged with blood. The venous sinuses showed this phenomenon to the most marked degree.

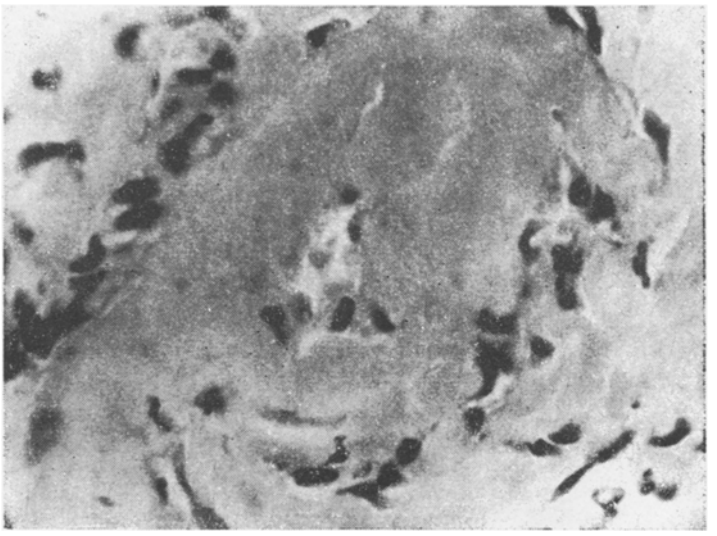

Fig. 1. Necrosis of the wall of an artery 22 days after sympathectomy. Photomicrograph. Hematoxylin-eosin. × 400.

Approximately 1 week after the operation and thereafter a series of morphological changes could be seen in the walls of the desympathized vessels.

Attention was first drawn to the marked edema of every layer of the blood vessel wall. The characteristic manifestation of edema of the blood vessels was the appearance of vacuoles of different sizes in the subendothelial layer. The cells of the blood vessels also developed vacuoles, notably the smooth-muscle cells of the tunica media. A characteristic feature of the muscular coat of the desympathized vessels was the unusual arrangement of the cell nuclei. In some arteries the nuclei of the muscle cells were concentrated in one part of the tunica media, so that most of this layer was devoid of nuclei. This alternation of nucleated and nonnucleated areas of the tunica media is a characteristic sign of the early changes caused by desympathization. Subsequently the nonnucleated areas began to occupy an increasingly larger area, the nuclei of the muscle cells disappeared, and where the muscular coat had been there remained a homogeneous, poorly stained substance. In rare cases necrosis of the vessel wall was observed (Fig. 1).

In the later periods of observation (6 months after the operation) the site of the necrotic vessel was occupied by a collection of connective-tissue cells, among which were a few cells resembling smooth-muscle cells in the shape of their nuclei (Fig. 2).

In the small arterioles the most conspicuous feature of the morphological picture of necrosis of the blood vessels was a disturbance of the correct orientation of the cells in all the layers of the vessel, often leading to obliteration of its lumen. The site of these empty blood vessels was occupied by bands of cells presenting a chaotic arrangement. The changes described in the arterioles resembled the pictures of regressive development of the precapillary arteries observed by S. I. Shchelkunov [5].

Besides disturbance of the orientation of the cells of the vessel wall, with death of the smooth muscles, in certain areas of the vessels intensive proliferation of the cells was observed. This proliferation was most marked in the intima. This increased proliferation of the intimal cells of the small blood vessels often led to complete obliteration of their lumen.

Thrombi were sometimes observed in the vessels of the desympathized skin, in various stages of organization. Morphological changes in the arrectores pilorum muscles consisted of polymorphism of the muscle nuclei and a characteristic alternation of areas with many nuclei and areas devoid of nuclei. Vacuolation of the muscle cells was often observed.

Cells outwardly resembling fibroblasts were often seen leaving bundles of smooth-muscle cells. This fact may probably indicate that the smooth muscle cells, when deprived of their sympathetic innervation, may turn into cells of the fibroblast type. Support for this hypothesis is given by the fact that in the later stages of the investigation nothing but groups of connective-tissue cells could be seen in places where bundles of smooth muscle are usually found.

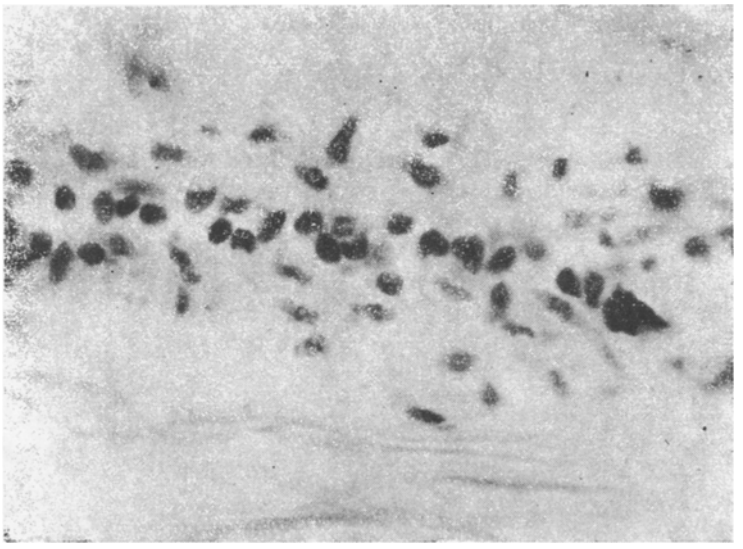

Fig. 2. Collection of cells at the site of a necrotic vessel 6 months after desympathization. Photomicrograph. Azure-II-eosin. × 400.

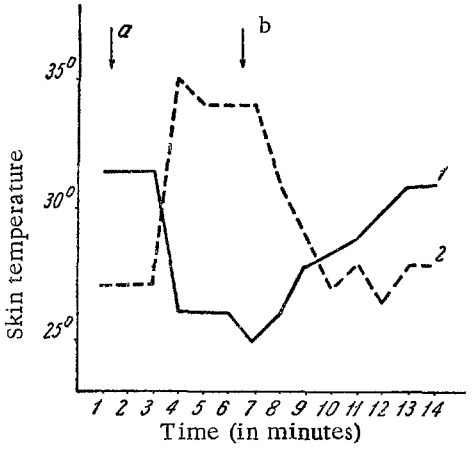

Fig. 3. Changes in the skin temperature of the desympathized ear during either anesthesia, 18 days after operation. 1) Experiment; 2) control; a) anesthesia applied; b) anesthesia discontinued.

The morphological changes in the skin glands consisted primarily of expansion of the sweat glands and an increase in the volume of the sebaceous glands. In some cases vacuolation of the secretory divisions of the sweat glands was observed.

Desympathization also caused other changes in the skin, although these were the result of the vascular disturbances and could be regarded as secondary. These changes include an increase in the number of connective-tissue cells in the edematous dermis, the appearance of perivascular zones of infiltration, and massive infiltration with mast cells, especially in the later periods of observation. At long intervals after the operation an increase was also observed in the number of cells in the epidermis and hair follicles undergoing mitotic division.

Measurement of the skin temperature showed that during the first 7-8 days after the operation the temperature of the desympathized ear was significantly higher than that of the control ear, the difference in temperature amounting to 7-10°. The difference subsequently became smaller and usually fell to 3-5°.

The reaction of the blood vessels of the desympathized ear to ether anesthesia, as determined by changes in the skin temperature, is of considerable interest. In the control ear ether anesthesia caused marked vasodilatation and, consequently, a marked rise in the skin temperature (by 7-10°). The reaction of the vessels of the desympathized ear to ether anesthesia was very different. During the first 7-8 days after sympathectomy ether anesthesia had no effect on the vessels of the desympathized ear and its skin temperature remained at the same high level. Later, when the temperature difference between the experimental and control ears diminished, not only did ether anesthesia not cause an increase in the skin temperature of the desympathized ear but, on the contrary, it caused a significant fall (Fig. 3). This type of reaction was observed in all the animals without exception (longest period of observation after sympathectomy 2 months). Besides the fall in the skin temperature of the ear, ether anesthesia also led to spasm of the muscles of the nictitating membrane and dilatation of the pupil on the side of the sympathectomy.

Analysis of the results shows that removal of the sympathetic innervation causes initially a marked dilatation of the blood vessels of the skin, expansion of the sweat glands, and an increase in the volume of the sebaceous glands. These phenomena are the result of exclusion of the motor innervation (with paralysis) of the smooth muscles of the vessels and of the myoepithelium of the glands.

Desympathization also gradually leads to structural changes in the smooth-muscle structures. In some cases these take the form of necrosis of the smooth-muscle cells, with their possible transformation into fibroblast-like cells. These processes in the muscular coat of the vessels, together with other morphological disturbances in the vessel wall (proliferation of the intima, thrombosis, edema) may in some cases lead to obliteration of the lumen of the vessel and to its necrosis.

However, necrosis of smooth muscle is only one of its possible reactions to desympathization. Many investigations by physiologists and clinicians have shown that when smooth muscle is deprived of its sympathetic motor innervation it is not only capable of contraction, but it also possesses increased sensitivity to mediators [9, 13]. The increase in the sensitivity of the smooth muscles to adrenalin may explain the fell in the skin temperature of the desympathized ear in response to ether anesthesia. Ether is known to cause hyperadrenalinemia, which leads to contraction of the desympathized smooth muscles of the vessels and also, consequently, to a fall in skin temperature. It should be noted that desympathized vessels do not react to administration of nembutal anesthesia, which does not cause hyperadrenalinemia [11]. There is no doubt that structural changes lie at the basis of this phenomenon of increased sensitivity of the smooth muscles to adrenalin. However, our experimental results do not provide a clear explanation of these changes.

It may be concluded that, besides causing disturbances of the nervous-reflex regulation of smooth muscle structures, in some cases desympathization may cause necrosis of blood vessels, of the arrectores pilorum muscles, and of the mycepithelium of the skin glands, and it may also give rise to increased sensitivity of the smooth muscle to adrenalin. This fact must be taken into consideration by surgeons using sympathectomy as a method of treatment of certain diseases.

SUMMARY

The skin of a cat's ear was studied morphologically at various periods after desympathization.

Skin temperature was measured by means of an electrothermometer prior to the experiment, at the time of desympathization and at various periods after it; the effect of ether anesthesia on the skin temperature was studied.

In a number of cases, besides the nervous-control disturbances, desympathization of smooth muscle formations also increased their sensitivity to adrenalin, beginning from the 7th-8th day.

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