ULTRASTRUCTURE OF THE FEMORAL ARTERIAL WALL IN RATS WITH CHRONIC REGIONAL ARTERIAL HYPOTENSION

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It is stated in the literature that prolonged regional arterial hypotension is accompanied by atrophic changes in the vessel walls [2, 5]. However, the fine structural changes taking place in arteries when the pressure in them is lowered has not been adequately studied.

Accordingly, in the investigation described below the ultrastructure of the femoral arterial wall was studied in rats with chronic regional arterial hypotension.

EXPERIMENTAL METHOD

Hypotension in the blood vessels of the hind part of the body was induced in noninbred male rats weighing 180-200 g by constricting the aorta with a nichrome coil, which was applied distally to the orifices of the renal arteries. In this way the blood pressure (BP) in the femoral arteries could be reduced by 30-50% [3]. The pressure in the cranial part of the aorta and its branches remained virtually unchanged.

In 13 animals (the controls and rats with arterial hypotention lasting 2, 12, 30, and 90-100 days) BP was measured in the carotid and femoral arteries under ether anesthesia, after which perfusion prefixation through the carotid artery was performed by the standard method [4]. Subsequent processing of the material was by the method described previously [1]. The semiautomatic Leitz—ACM system was used to measure the thickness of the muscular layers and intermuscular spaces and for statistical analysis of the data.

EXPERIMENTAL RESULTS

No signs of descending inflammation or descending degenerative changes could be found in the wall of the caudal part of the aorta in any of the animals.

In the control rats the femoral arteries had the appearance of blood vessels of muscular type with a well-developed inner elastic membrane (IEM) 0.55 ± 0.1 μ thick (M ± σ) and with seven or eight layers of smooth muscle cells (SMC) separated by bands of ground substance with collagen and a few elastic fibers. The mean thickness of each muscular layer was 4.04 ± 0.4 μ and of the intermuscular spaces 0.84 ± 0.11 μ.

Examination of semithin sections showed that in longitudinal sections of the SMC their pointed ends had an internal angle of close to 45°. The terminal portions of SMC, lying in one layer, often did not overlap one another but were separated by a space filled with ground substance, collagen fibers, processes of SMC of varied thickness (Fig, 1a, b), and accumulations of special structures including small and large vesicular formations, from 20 to 200 nm in diameter, multivesicular and myelin-like bodies, granules, and clumps of material (Fig. 1a, e). These structures have been described as "extracellular matrix vesicles" [6, 7]. Close to these vesicles, usually arranged among the collagen fibers, including in the intermuscular spaces, undoubted fragments of the SMC islets could be seen, although they no longer had the basement membrane which, as a rule, surrounds each myocyte. The basement membrane of SMC in some parts was stratified (Fig. 1d), and this is usually regarded as evidence of migration of the cells and their processes.

KEY WORDS: regional arterial hypotension; femoral artery; smooth muscles; extracellular vesicles.

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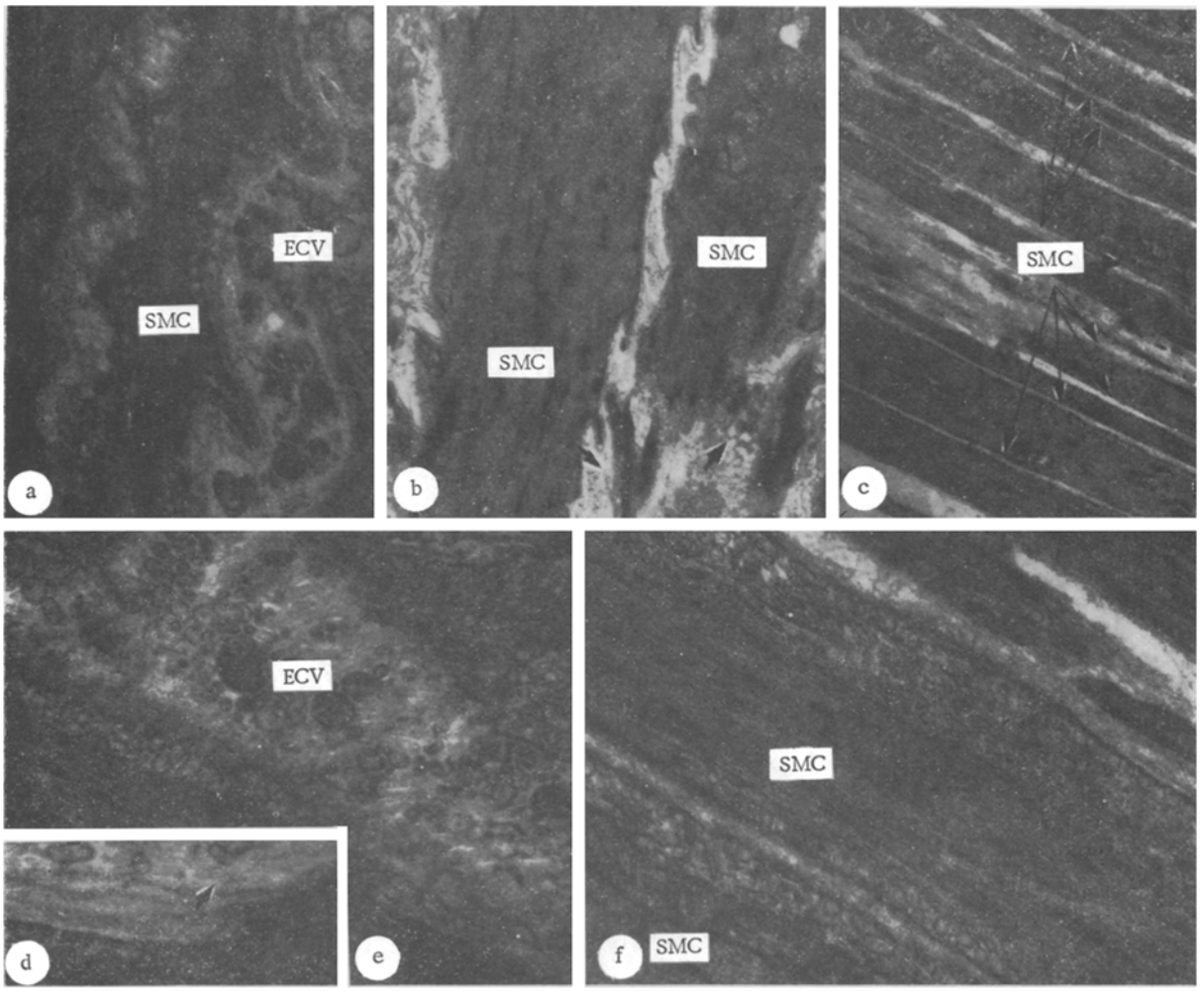

Fig. 1. Details of ultrastructure of muscular coat of femoral artery of control rats (a, b, d, e) and animals with arterial hypotension for 12 h (c, f). a) Process of SMC surrounded by basement membrane, and extracellular vesicles (ECV) of different sizes and shapes; b) fragment of cytoplasmic part of SMC with processes (arrow); c) fragments of SMC after hypotension for 12 days; d) stratified basement membrane of SMC (arrow); e) ECV together with fragment of SMC. Fragment (*) has no clearly defined basement membrane; f) zone occupied by vesicles and endoplasmic reticulum in myocyte from femoral artery of rat with hypotention lasting 12 days, under higher power. Magnification: a) 34,200: b, c) 4680: d, e) 57,000: f) 38,000.

The ultrastructure of the femoral arterial wall 2 days after lowering of BP was practically normal. Only some thickening of IEM to 1.23 ± 0.07 μ together with some decrease in the thickness of the endothelial lining could be noted.

However, 12 days after construction of the aorta marked ultrastructural changes were found in the wall of the femoral artery. In both semithin and ultrathin sections the thickness of the muscle coat was considerably reduced (to 14-15 μ; in the control rats 34-40 μ). The thickness of the endothelial lining and of IEM showed no significant change. The decrease in thickness of the media was due both to narrowing of the intermuscular spaces (to 0.42 ± 0.05 μ; $P < 0.01$) and to a decrease in thickness of the myocytes, whose diameter was almost halved to reach 1.53 ± 0.2 μ. Not only were myocytes reduced in thickness, but they were also considerably stretched, the terminal portions of SMC in some cases continued one after another for a long distance, and consequently the number of muscular layers in the wall of the femoral artery during this period was increased to 10-11. The configuration of the terminal portions of SMC also was modified: Their internal angle was reduced to 10-15° and the processes and extracellular vesicles completely disappeared (Fig. 1c, f). The lumen of the artery at this period was increased by 20-30% compared with the control. The structure of SMC also was changed (Fig. 1f). The nuclei of SMC became thinner and much of the periph-

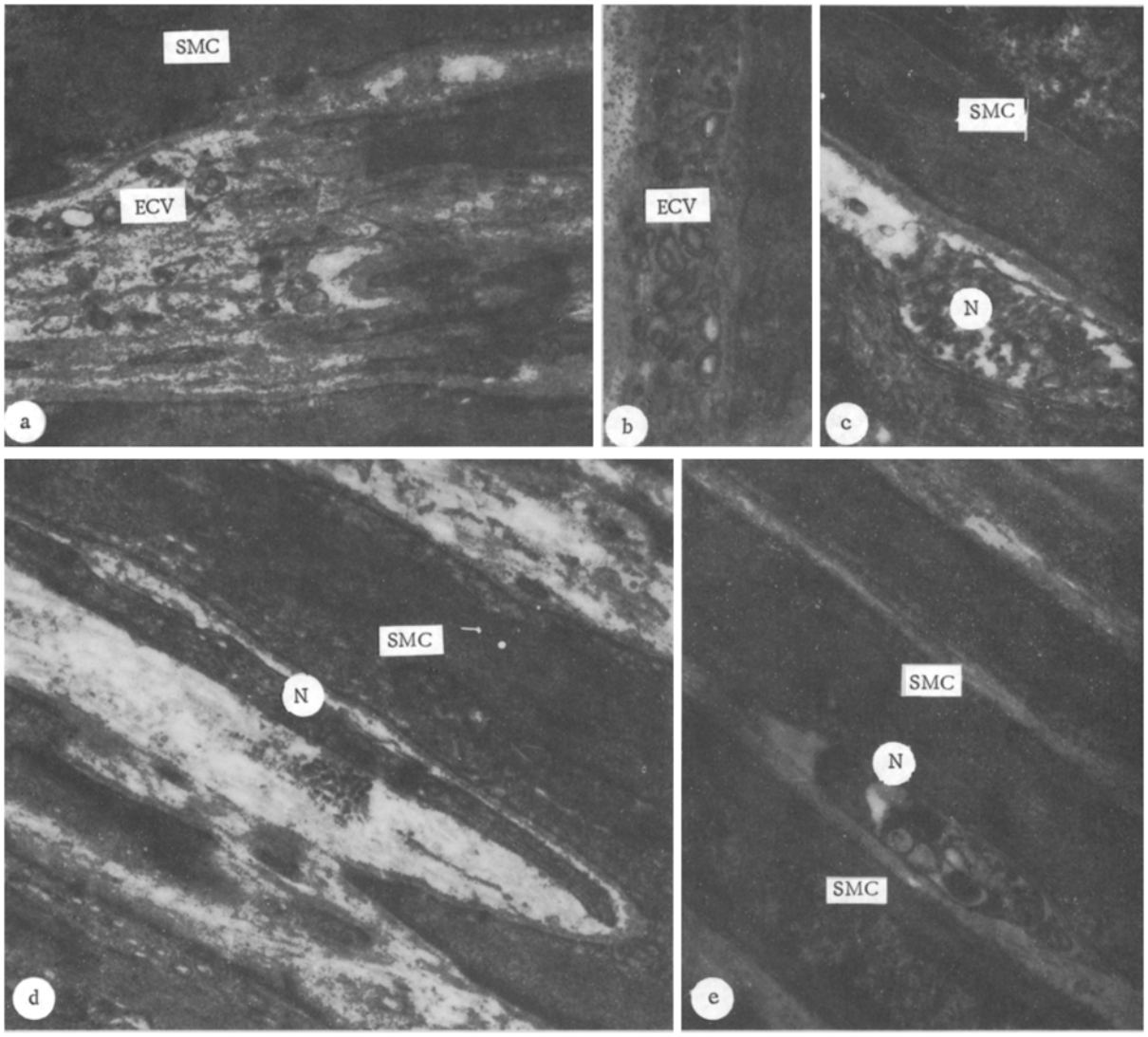

Fig. 2. Details of ultrastructure of muscular coat of femoral artery of rats with arterial hypotension lasting 30 days (a, b) and 12 days (c, d, e). a, b) Processes of SMC and ECV; c) bare axon with varicose expansion containing small vesicles; d, e) nerve fibrils among layers of SMC. Magnification: a) 31,050; b) 41,400; c) 57,000; d) 38,000; e) 28,500. BM) Basement membrane; N) nerve.

eral part of the myocytes was filled with vesicles and collapsed tubules of the smooth and rough endoplasmic reticulum (Fig. 1f). Bundles of microtubules appeared in some SMC.

During this period thin bundles of unmyelinated axons were found in the outer third of the muscle coat of the femoral artery between the muscle layers (Fig. 2d, e), sometimes with varicose expansions containing small and partly granular vesicles (adrenergic). In the control animals and in rats with hypotension of different durations, unmyelinated nerves, including those with vesicular axons, were seen only close to the outer boundary of the media. No significant changes were found in the structure of the nervous apparatuses in the animals subjected to this operation (Fig. 2c).

A study of semithin sections of material taken from animals with hypotention lasting 30 days showed that, much as in the control rats, the myocytes were fusiform in shape, although they were much thinner than normal myocytes (the mean thickness of the muscular layers in the experimental rats was 2.2 ± 0.2 μ; $P < 0.01$). Restoration of the shape of the SMC was accompanied by reappearance of their processes; meanwhile extracellular vesicles reappeared in the intermuscular spaces (Fig. 2a, b). Admittedly extracellular vesicles were found much less frequently than in the control animals. The number of muscular layers in the wall of the femoral artery was seven or eight, just as in the control rats. The thickness of the intermuscular spaces was reduced by half as before. The muscular coat as a whole remained thin.

The structure of the femoral arterial wall after 90-100 days resembled that observed in rats with hypotension lasting 30 days: The number of processes of SMC and of extracellular bodies was reduced, the SMC were thinner, their structure was uniform and they contained no organelles.

As a result of the decrease in BP the wall of the femoral artery was thus sharply reduced in thickness due to a decrease in diameter and increase in length of the SMC and also to narrowing of the intermuscular spaces. Some increase in the lumen of the vessels was observed. Although no gross damage to the myocytes was found in the wall of the femoral artery they lost their processes and the extracellular vesicles disappeared in the media. This phenomenon is interesting in the light of data in the literature linking certain forms of thinning of the vessel wall with the function of these particular formations, some of which contain lysosomal enzymes [6, 7]. The possibility cannot be ruled out that disappearance of the extracellular vesicles in the wall of the femoral artery of animals with hypotension signifies liberation of their contents (including enzymes) into the substance of the muscular coat and contributing to a decrease in its thickness.

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