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SKELETAL MUSCLE MORPHOLOGY IN ALLOXAN DIABETES

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KEY WORDS: alloxan diabetes; skeletal muscle; morphology.

Many new facts on diabetes have been discovered in recent years, on the basis of which it can be concluded that diabetes mellitus is a polypathogenetic disease, in which an absolute or relative insulin deficiency gives rise to functionally expressed morphological disturbances of many organs and systems [2, 3].

Among patients with ischemic lesions of the lower limbs the largest group consists of diabetics, in whom the incidence of gangrene is 40 times greater than in patients with atherosclerosis alone. Diabetic gangrene of the lower limbs is not only, and not so much a manifestation of atherosclerotic changes in major blood vessels, as the result of a lesion involving vessels of the microcirculatory bed [1, 4, 5].

In the few morphological studies which have been made of skeletal muscles in diabetes, microangiopathies have been found, with a lesion of the vessel walls and of their basement membranes. These changes are particularly marked in patients with insulin deficiency in a state of decompensation, with which is associated the development of mechanical changes in vascular permeability and dystrophic and sclerotic changes in the tissues [6-8].

The aim of this investigation was to study the structural basis of the skeletal muscular lesion in animals on an experimental model of alloxan diabetes (AD).

EXPERIMENTAL METHODS

Experiments were carried out on 12 mongrel dogs of both sexes weighing 9-22 kg. Diabetes was produced by a single intravenous injection of 10% alloxan (80 mg/kg). The development of diabetes was confirmed by determination of the blood sugar by the Hagedorn–Jensen method. After the clinical data showed development of long-lasting AD, with a duration of 2, 3, 4, and 5 months, the animals were killed by intracardiac injection of hexobarbital. Pieces of skeletal muscle from the rectus abdominis muscle and a superficial thigh muscle were taken for morphological study.

The pieces of muscle for light-optical investigation were fixed in 10% neutral formalin and embedded in paraffin wax; sections were stained with hematoxylin and eosin, by Van

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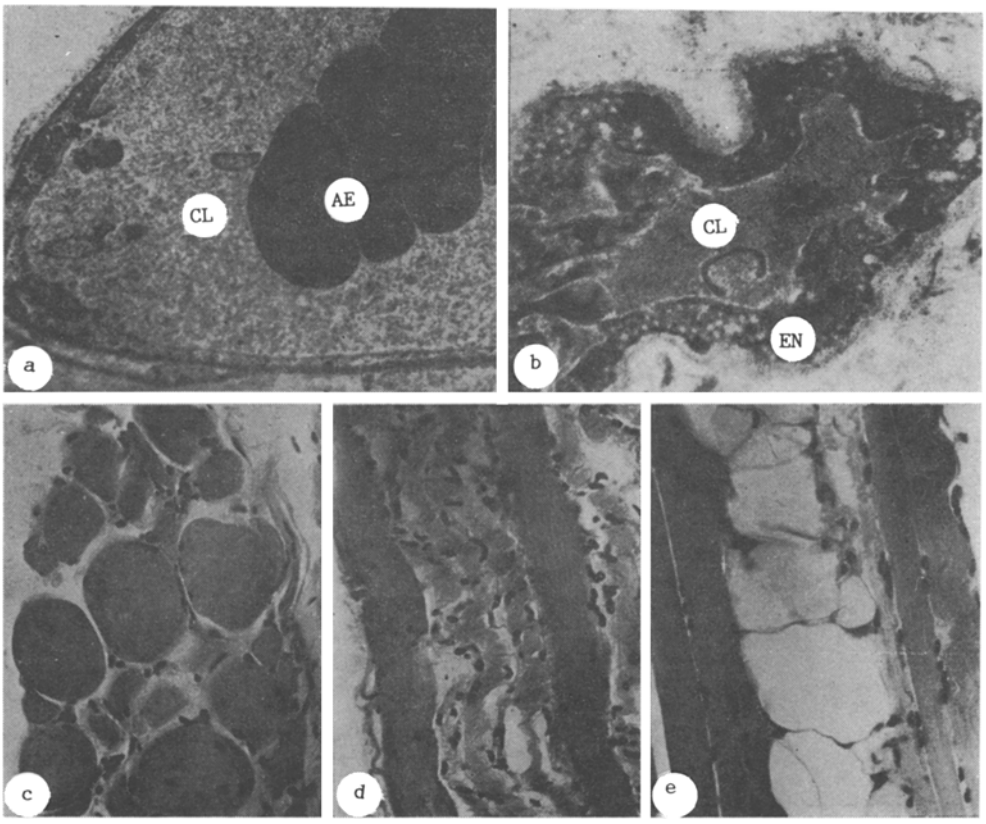

Fig. 1. Electron-microscopic (a, b) and histologic (c, d, e) changes in skeletal muscle in AD. a) Aggregated erythrocytes (AE) in capillary lumen (CL). 10,000×; b) Numerous pinocytotic vesicles in cytoplasm of endotheliocyte (EN), loosening of basement membrane (BM) of capillary. 14,000× c, d) Muscle fibers differing in thickness and tortuosity. Hematoxylin and eosin. 400×; e) Adipose tissue along course of endomycial sheaths. Hematoxylin–eosin. 400×.

Gieson's and Mallory's methods, and by the PAS reaction. Pieces of tissue for electron microscopy were fixed in a 2.5% solution of glutaraldehyde or a 1% solution of osmic acid, and embedded in Araldite. Semithin sections were first cut and stained with methylene blue and azure, after which ultrathin sections were cut and stained with silver nitrate. The ultrathin sections were studied under the EMV-100B electron microscope.

EXPERIMENTAL RESULTS

The regular fascicular structure of the skeletal muscles was preserved in different groups in animals with AD lasting 2-3 months, on histologic examination. Muscle fibers in transverse and longitudinal sections were of uniform diameter. In longitudinal sections dark and pale muscle fibers with clear cross striation and with large nuclei regularly distributed beneath the sarcolemma were found in the composition of the bundle. The sarcolemma had mainly even outlines and invaginations, and it could be identified only in the nuclear zones. Its outlines were emphasized mainly by PAS-positive permeation of the basement membrane of the muscle fiber. Numerous congested capillaries and venules were seen in the widened, edematous intercellular spaces. Only solitary mononuclears and bundles of collagen could be seen in the loosened layers of endomysium.

On electron-microscopic investigation of the intermuscular capillaries, the changes observed in the structure of the endotheliocytes indicated increased pinocytotic activity and thickening and loosening of the basal layer. Aggregated erythrocytes were seen in the dilated lumen of individual capillaries (Fig. 1a, b). The pericapillary spaces were widened and filled with fragmented collagen fibrils, preserving contact with the basement membrane of the vessels only in certain areas.

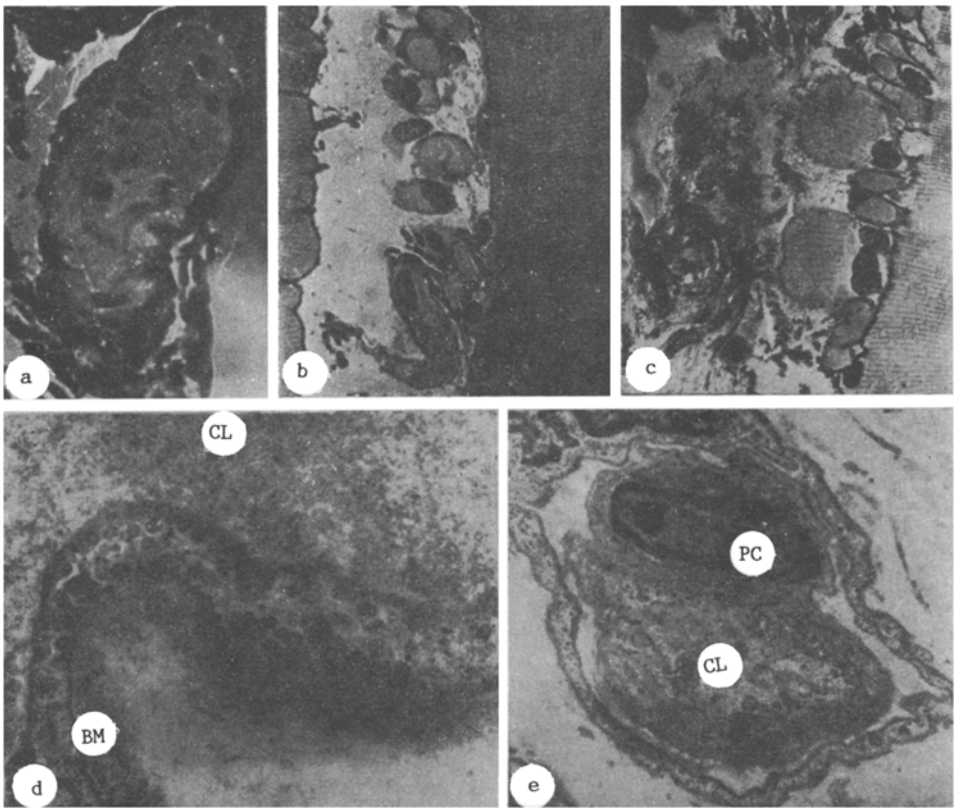

Fig. 2. Histologic (a, b, c) and electron-microscopic (d, e) changes in skeletal muscle in AD of 4-5 months' duration. a) Arteriole with narrow lumen, hypertrophy of wall, and perivascular sclerosis. Semithin section. Stained with methylene blue and azure. 900×; b, c) swelling of sarcoplasm of myocytes, numerous capillaries of endomysium, and intermuscular sclerosis. Semithin sections. Methylene blue — azure. 900×; d) Thickening of basement membrane (BM) of capillary. 32,000×; e) Narrowing of capillary lumen (CL), hypertrophy of pericytes (PC). 12,000×.

After 4-5 months signs of dissociation of the bundles of muscle fibers were observed, with wide intervening layers of loose connective and adipose tissue. The muscle fibers in bundles differed in thickness because of hypertrophy of some and atrophy of others (Fig. 1c, d). Pale muscle fibers with irregular eosinophilic areas of cytoplasm predominated. Diffuse growth of adipose tissue were observed throughout the bulk of the muscles. Adipose cells were often observed inside old endomysial sheaths, replacing muscle fibers (Fig. 1e). The outlines of the sarcolemma were festooned in appearance because of multiple focal invaginations of the sarcoplasm in the extra- and perinuclear zones (Fig. 2c).

Moderately congested blood vessels and dilated lymphatics were located in perimysial membranes. The arterioles were characterized by thickening of the walls and narrowing of their lumen. The vessel walls were thickened because of hypertrophy of the endotheliocyte nuclei, proliferation of smooth-muscle and adventitial cells, and also perivascular sclerosis (Fig. 2a). Numerous capillaries with proliferation of pericytes and of connective and adipose tissue cells were seen in the endomysium (Fig. 2b, c).

The basement membranes of the capillaries and myocytes were thickened and histochemically they gave a positive PAS reaction.

Diffuse thickening of their basement membrane was found in the intermuscular capillaries under the electron microscope. They became homogeneous and structureless, and in thickness they often exceeded the cytoplasmic processes of the endotheliocytes. The number of micropinocytotic vesicles was reduced in the cytoplasm of the latter cells, and they were preserved only near the plasma membranes (Fig. 2d). The walls of individual capillaries were thickened

on account of hypertrophy of the pericytes and perivascular connective tissue cells, sometimes surrounding the capillary in a ring. The lumen of these vessels was constricted and the pinocytotic activity of the endothiocytes reduced (Fig. 2e).

Ultrastructural study of the myocytes in areas of subsarcolemmal invaginations revealed separation and partial lysis of the myofibrils. Numerous lipid inclusions were found in other muscle fibers beneath the sarcolemma and in the thickness of the fiber.

The changes in the skeletal muscle of the experimental animals revealed histologically, histochemically, and electron-microscopically, when related to the duration of AD, thus indicate that changes in vessels of the microcirculatory bed correspond to those typical of diabetic microangiopathies. They are manifested as increased vascular permeability, congestion, intravascular aggregation of erythrocytes, and perivascular and tissue edema. In long-standing diabetes, these changes are joined by thickening of the vascular walls due to widening of the basement membranes and their permeation by PAS-positive material, and hypertrophy of the pericytes and smooth-muscle and adventitial cells. Ofter these changes are accompanied by a decrease of vascular permeability. Changes described in the muscle fibers are observed only in the case of long-standing AD and they are most probably secondary, caused by disturbances of the microcirculation and of vascular permeability. Proliferation of adipose tissue resembles the deposition of fat in vacant spaces when lipid metabolism is disturbed in AD.

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COMPENSATORY AND REPAIR PROCESSES IN THE THYROID GLAND OF MONTH-OLD DESYMPATHIZED RATS

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It is well known that proliferative activity of the thyroid parenchyma is induced by hypothalamic influences through thyrotrophin (TSH), secreted by the adenohypophysis [4, 7, 9]. This pathway is not the only possible mode of action on mitotic activity of the thyroid epithelium, which is certainly under the control of other regulatory factors [1, 3, 5, 10]. Every year our ideas on the character of the course of thyroid gland (TG) regeneration in different functional states of the autonomic nervous system are widened. However, insufficient attention has been paid to the study of the role of the sympathetic nervous system,

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