MYELIN-LIKE STRUCTURES IN HEART MUSCLE CELLS AFTER ADMINISTRATION OF ADRENALIN

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UDC 612.172.014.2.014.46 : 615.357.452

The state of the heart muscle cells of 36 albino rats was studied experimentally after a single intramuscular injection of adrenalin hydrochloride (3 mg/kg) into the thigh. Electron-microscopic investigation of the heart muscle cells showed foci of overcontraction and overstretching of the myofibrils, as well as numerous myelin-like figures, often containing mitochondria and glycogen, and drops of lipids. It is postulated that the harmful action of adrenalin is manifested through the activation of lipolysis, leading to dissociation of the protein–lipid components of the mitochondrial membranes, the accumulation of fatty acids in the cytoplasm, and resynthesis of new and unusual membrane formations.

KEY WORDS: adrenalin; myocardium; lipid metabolism.

The state of the heart muscle cells under the influence of adrenalin has been described in detail on several occasions [1-3, 6]. Contractural changes in the myofibrils, considered to lead to focal necrosis of the myocardium, have been studied in the greatest detail. Tsellarius and Semenova [6] distinguished a special type of injury to the muscle cells, known as myocytolysis. In their opinion focal lysis of the myofibrils takes place through sudden activation of acid hydrolases and the massive formation of lysosomes. Meanwhile, electron-microscopic investigations of the myocardium after administration of adrenalin in various doses have not revealed the decisive role of lysosomes in the formation of destruction of the contractile system of the myocytes [4, 7, 17]. The mechanism of injury to the heart muscle cells in the presence of excess of adrenalin has not been adequately explained.

The object of this investigation was to study the state of the ultrastructure of the heart muscle cells at a time of functional stress of the myocardium during the development of cardiovascular failure.

EXPERIMENTAL METHOD

Experiments were carried out on 150 noninbred albino rats weighting 200 g. A solution of adrenalin hydrochloride was injected intramuscularly (into the thigh) in a concentration of 1 : 1000 and a dose of 3 mg/kg. On the second day after the single dose of adrenalin 36 rats developed manifestations of cardiovascular failure: marked dyspnea, severe tachycardia, and adynamia. The animals were decapitated. Pieces of myocardium from the left ventricle were fixed in 1% OsO_4 solution by Caulfield's method, dehydrated, and embedded in Araldite. Electron micrographs were prepared in the IEM-100B microscope.

EXPERIMENTAL RESULTS

Two types of processes were clearly observed in the myocardial muscle cells of rats with signs of cardiovascular failure on the second day after injection of adrenalin: degenerative and regenerative.

The degenerative processes in the heart muscle cells evidently largely determined the severity of the clinical picture following administration of adrenalin. Electron-microscopic examination revealed mul-

Department of Pathological Anatomy, Stomatological Faculty, N. A. Semashko Moscow Medical Stomatological Institute. (Presented by Academician of the Academy of Medical Sciences of the USSR A. P. Avtsyn.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 80, No. 11, pp. 101-105, November, 1975. Original article submitted February 4, 1975.

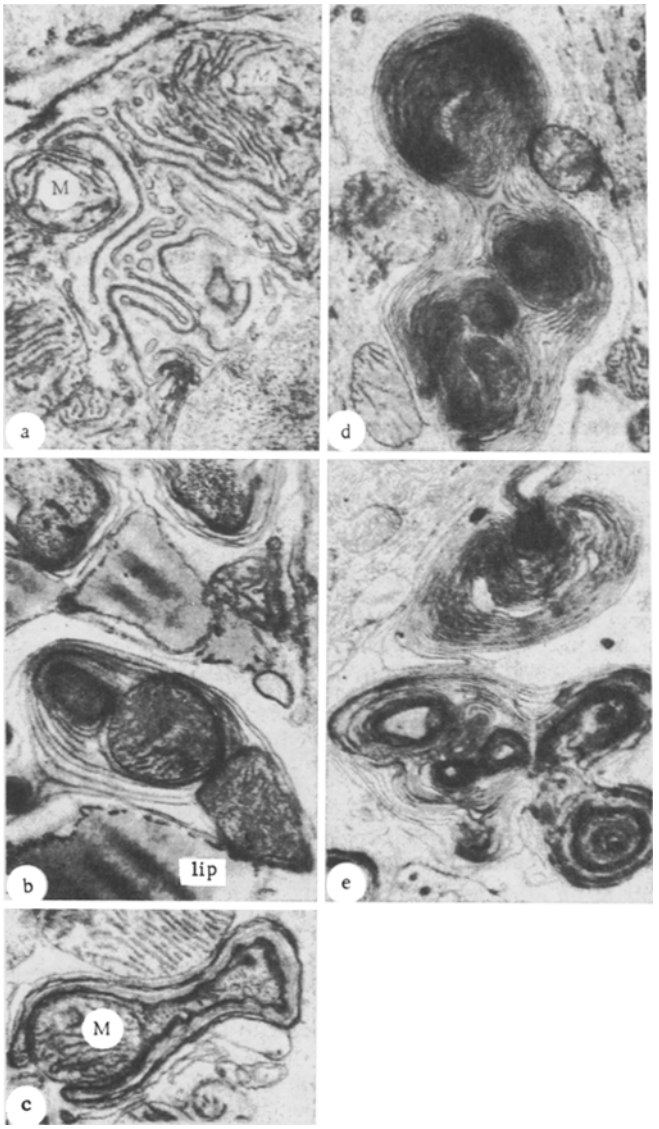

Fig. 1. Formation of myelin-like structures in heart muscle cell: a) distribution of mitochondria (M) on cisterns and tubules (20,000 ×); myelin-like structure "creeping" over a mitochondrion (28,000 ×); c) drops of lipids (lip) near myelin-like figures (25,000 ×); d) giant myelin-like structures in muscle cell (20,000 ×); e) myelin-like structures in extracellular space (18,000 ×).

tiple foci of overcontraction and overstretching of the myofibrils in the muscle cells and lipids were abundant in the cytoplasm. The myofibrils and myofilaments in a state of overcontraction lost their regular orientation and became osmiophilic, dense, and homogeneous. Conversely, in the foci of overstretching of the myofibrils disappearance of the contractile elements was observed in some places and only occasional myofilaments were regularly arranged along the long axis of the cell. The structure of the sarcomeres was indistinguishable.

In the zone of overstretching of the myofibrils and also beneath the sarcolemma marked changes were observed in the mitochondria. Often the mitochondria appeared to have lost their outer membrane and to be "scattered" into separated closed cisterns, tubules, and vesicles (Fig. 1a). Some of the tubules surrounded the nearby mitochondria in a semicircle. In some cases the cisterns and tubules were flattened and formed double-contoured myelin-like structures. Myelin-like figures were very often found close to drops of lipids (Fig. 1c). Sometimes intimate contact was found with membranes 60-70 Å in thickness which seemed to emerge directly from the lipid drops. Double membranes formed complex concentric figures,

often consisting of 15-20 layers. A regular feature was that these "myelin" structures seemed to envelop individual mitochondria (Fig. 1b) and to immure them. In most cases a variable number of glycogen granules was found between the myelin-like membranes and the mitochondria enclosed in them. Gradually the double membrane formations completely surrounded the mitochondria, the structure of which was considerably disturbed: Obliteration of the outlines of the cristae and increased osmiophilia of the matrix were observed.

In some cases the myelin-like structures attained a considerable size, namely 15-20 μ in diameter (Fig. 1d) and were found in the extracellular space (Fig. 1e). Cells of macrophagal type were frequently found in their neighborhood.

The changes in the ultrastructure of the heart muscle cells during the development of cardiovascular failure caused by injection of adrenalin, as described above in the form of multiple foci of overcontraction and overstretching of the myofibrils, considerable changes in the mitochondrial membranes, the formation of multiple concentric myelin-like structures, and the appearance of drops of lipids in the cytoplasm, can thus be regarded as a manifestation of degenerative processes.

The foci of overcontraction and overstretching of the myofibrils observed in these experiments were evidently due to an increase in the concenteation of free calcium in the cytoplasm of the muscle cells through a decrease in ATPase activity of the sarcotubular system resulting from the action of adrenalin [9]. These findings are in agreement with the results of electron-microscopic investigations by Mitin and Beskrovnova [4], David et al. [7], Wenzel et al. [17], and others.

The presence of numerous myelin-like structures with mitochondria embedded in them, discovered in these experiments in the cytoplasm of the muscle cells of the ventricles, correlates with the results of light-optical studies by Danilova [2] and Tsellarius and Semenova [6]. The first worker cited, who studied adrenalin myocarditis, observed distinctive granules in certain parts of the muscle fiber and regarded them as swollen sarcosomes. The two last workers, 40-60 min after injecting adrenalin, by means of a combination of polarization and phase-contrast microscopy, found granules of different sizes and densities in zones of what they described as myocytolysis, and which in their opinion bore all the signs of mitochondria. Some of these granules were basophilic on staining, others fuchsinophilic. Their reaction for acid and alkaline phosphatases was negative, but individual granules gave a positive reaction for succinate dehydrogenase and they stained weakly in the reaction for tryptophan.

The myelin-like figures observed in the present experiments in zones of disorganization of the contractile structures of the muscle cells evidently correspond to the granules described by Danilova and by Tsellarius and Semenova [2, 6].

What is the nature of formation of these myelin-like structures, not normally found in myocytes, in the cytoplasm of the muscle cells? Catecholamines and, in particular, adrenalin are known to cause activation of lipolysis and, correspondingly, of lipases which stimulate mobilization of nonesterified fatty acids from adipose tissue [8]. Under the influence of adrenalin phospholipase A, the only phospholipase present in mitochondria, is evidently activated [10, 13, 15, 16]. This, in turn, may lead to hydrolysis of the phosphatides of the mitochondrial membranes. Phospholipase A has been shown to hydrolyze the membrane phosphatidylethanolamine, with a resulting increase in the content of lysophosphatidylethanolamine and fatty acids in the cytoplasm [11, 14]. Meanwhile resynthesis of phosphatidylethanolamine – one of the most important structural and functionally active phosphatides of membranes [5] – is also possible.

The increase observed in the number of lipid drops and the presence of myelin-like structures are an expression of the indirect action of adrenalin on the mitochondrial membranes, causing dissociation of their protein–lipid structural components and, at the same time, the resynthesis of new and unusual membrane formations, reflecting profound degenerative changes and, in particular, a disturbance of lipid metabolism.

The foci of overcontraction and overstretching of the myofibrils detected in the muscle cells, the presence of numerous myelin-like structurs and lipid drops in the cytoplasm, and the destruction of individual mitochondria reflect marked degenerative processes in the myocardium under the influence of adrenalin and they are among the factors responsible for cardiovascular failure.

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