ADRENALIN-INDUCED MYOCARDIAL LESIONS IN GENETICALLY HYPERTENSIVE RATS

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UDC 612.12-008.331.1:591.15:
616.24-005:615.711.7

KEY WORDS: genetic hypertension; stress; adrenalin-induced myocardial lesions; membrane permeability.

Several experimental models of genetic hypertension in rats have now been obtained. From the standpoint of interaction between genotype and environment in the formation of arterial hypertension these models can be divided into two groups: lines of animals with spontaneously elevated arterial pressure, which is virtually independent of environmental influences (lines SHR, MHS, LH, and GH), and lines of rats in which a hereditary predisposition to hypertensive states is realized under certain environmental conditions and, in particular, during the action of DOCA or sodium chloride (lines DS, SBH; the names of the lines are in accordance with the international nomenclature [12]).

One of us (A.L.M.) first obtained an experimental model of genetic hypertension, the development of which is largely due to the action of emotiogenic stimuli, by selection on the basis of autobred Wistar rats [1]. The hereditary predisposition is manifested by the fact that during mild emotional stress a considerable rise of blood pressure is observed in virtually all the animals. In male rats of the 11th generation the mean arterial pressure was 184 ± 3.9 mm Hg (in the original population the corresponding figure was 128 ± 2.0 mm Hg) [1].

This paper gives the results of investigation of genetically determined functional aspects of the cardiovascular system in the genetically hypertensive rats which we obtained. In particular, a very interesting question is that of the sensitivity of the myocardium to the action of stress hormones, including adrenalin, more especially because essential hypertension is recognized as one of the leading risk factors increasing the probability of development of myocardial infarction [6].

EXPERIMENTAL METHOD

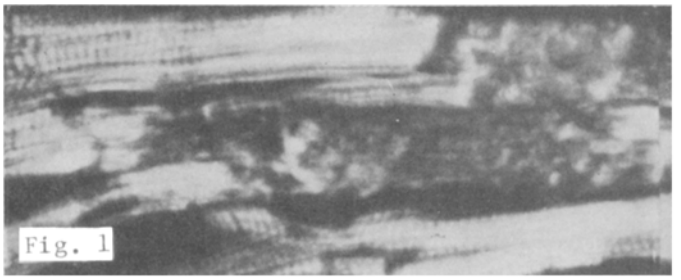
Experiments were carried out on 35 rats aged 9 months: 15 genetically hypertensive animals and 20 normotensive autobred Wistar rats. The experimental animals were given a single subcutaneous injection of 0.1% adrenalin solution in a dose of 5 ml/100 g body weight; the control animals received the same volume of isotonic sodium chloride solution. From the group of hypertensive rats 10 animals were used in the experiment, and from the group of normotensive Wistar rats 12 were used; five and eight rats respectively served as the control. All the animals were decapitated after 24 h, the heart was stopped by cold and fixed with 4% buffered formaldehyde. Paraffin sections, stained with hematoxylin and eosin and by the colloidal iron—PAS—hematoxylin—orange method [8], were examined in ordinary and polarized light. The degree of damage to the myocardium was determined in numbered preparations and expressed in points: 0) no lesions; 1) damage to single cells in the preparation; 2) infrequent small foci consisting of a few cells; 3) small foci consisting of several cells; 4) large focal lesions resembling infarcts. Two types of lesions were assessed separately: intracellular monocytolysis and coagulation necrosis of cardiomyocytes [9]. To assess the significance of of differences, the Wilcoxon—White nonparametric test [5] was used.

Institute of Cytology and Genetics, Siberian Branch, Academy of Sciences of the USSR, Novosibirsk. (Presented by Academician of the Academy of Medical Sciences of the USSR D. S. Sarkisov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 99, No. 3, pp. 356-358, March, 1985. Original article submitted June 15, 1984.

 0007-4888/85/9903-0360$09.50 © 1985 Plenum Publishing Corporation

TABLE 1. Assessment of Severity of Myocardial Lesions in Hypertensive and Normotensive Rats 24 h after Injection of Adrenalin (0.5 ml of 0.1% solution/100 g body weight)

Type of lesion	Group of animals	Assessment in points					Mean rating, points
		0	1	2	3	4	
Coagulation necrosis	Normotensive (n = 12)	4	4	—	4	—	1,3
	Hypertensive (n = 10)	—	—	2	4	4	3,2
Intracellular myocytolysis	Normotensive (n = 12)	1	5	1	5	—	1,8
	Hypertensive (n = 10)	2	1	3	4	—	1,9



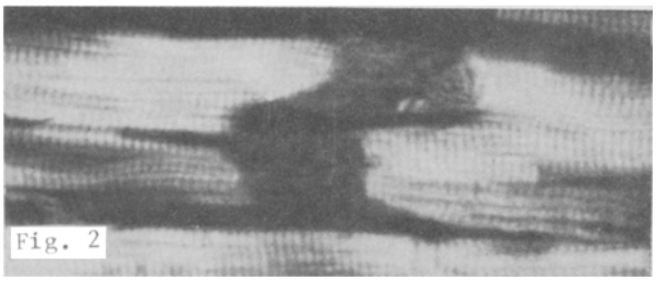


Fig. 1. Cloudy-swelling degeneration of myofibrils in cardiomyocytes in coagulation necrosis. Here and in Fig. 2: photograph in polarized light. 800×.

Fig. 2. Foci of lysis of myofibrils in cardiomyocytes in intracellular myocytolysis.

EXPERIMENTAL RESULTS

In all animals receiving adrenalin characteristic focal lesions were found in the myocardium [8]. These lesions fall into two types. The first is coagulation necrosis developing on a basis of contractural injuries of the II and III degree, and cloudy-swelling degeneration of myofibrils (Fig. 1). In cells with lesions of this type a positive PAS reaction, not inhibited by amylase, appears, evidence of plasma imbibition of these cells [7]. In polarized light, at this stage of the process cloudy-swelling degeneration of the myofibrils is most frequently found. Coagulation necrosis of cardiomyocytes induces a response of the stroma, in the form of mucoid edema, revealed by the reaction with colloidal iron, and also accumulation of macrophages and leukocytes. The second type of lesion observed, intracellular myocytolysis (Fig. 2), is detectable by polarization microscopy. The changes consist essentially of lysis of myofibrils, which in most cases is reversible [4]. At the stage when this investigation was carried out, mainly intracellular myocytolysis in the regeneration stage was observed. The reaction of the stroma around foci of this type is minimal.

The results of assessment of the severity of myocardial damage in animals of the two experimental groups after injection of adrenalin are given in Table 1. They show that as regards the degree of spread of coagulation necrosis, changes were more severe in hypertensive rats ($P < 0.01$). So far as intracellular myocytolysis is concerned, no significant difference could be found between the groups of animals. In control animals of both groups no necrobiotic changes or intracellular myocytolysis were found.

It must be emphasized that the mechanisms of development of contractural lesions terminating in coagulation necrosis and in intracellular myocytolysis are different. Coagulation necrosis is connected with a disturbance of membrane permeability and is accompanied by plasma imbibition of the cells [3, 7, 10, 11]. Meanwhile intracellular myocytolysis never leads to plasma imbibition and it evidently arises as a result of acidification of the intracellular medium and activation of acid hydrolases as a result of disturbance of cell respiration [4]. In this connection it should be noted that Postnov and Orlov [2] found that the formation of genetically determined hypertension is SHR rats is connected with a genetically determined disturbance of the structure of the biological membranes.

It can be concluded from these results that increased sensitivity of the mycocardium to the harmful action of adrenalin is present in the rats investigated, which are characterized by genetically determined hypertension provoked by stress; it is manifested only in relation to types of lesions connected with a disturbance of permeability of the cardiomyocyte sarcolemma. The molecular-genetic and physiological bases of this phenomenon will be elucidated by future investigations.

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LIPID GRANULARITY AND TOPOGRAPHIC FEATURES OF RENOMEDULLARY INTERSTITIAL CELLS IN SPONTANEOUSLY HYPERTENSIVE RATS

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UDC 616.12-008.331.1-055.5/.7-07:616.61-008.939.15

KEY WORDS: kidneys; renomedullary interstitial cells; spontaneous hypertension.

The interstitial cells (IC) of the renal medulla have been shown [13, 14] to possess internal secretory activity and, in particular, to produce prostaglandins (PG). However, it is not clear how important is the role of renomedullary IC (RMIC) in the general system of arterial pressure regulation. Potentiation of synthesis of renal PG during arterial hypertension [2, 11] is evidence of activation of the antihypertensive function of the renal interstitial tissue.

The electron-microscopic picture of RMIC in different types of hypertension in rats has now been described in fair detail [3, 5, 10]. Nevertheless, the admitted limitation of the material which can be studied by electron microscopy prevents consideration of the topography of the renal medulla as a whole. The zonal structure of the renal papilla, for instance, is heterogeneous in both vertical and horizontal directions. Consequently, there is reason to assume that in this case a light-optical study will be sufficiently acceptable. In some cases [7, 9, 12] it has been found possible to study the morphological and functional state of IC on the basis of indirect data, namely the concentration of the lipid granules. As has been shown [6], blocking synthesis of PG and storage of their precursors (mainly triglycerides of unsaturated fatty acids) leads to accumulation of lipid granules in the cytoplasm of IC and to an increase in their volume.

The aim of this investigation was to study the concentration of lipid granules in RMIC in spontaneously hypertensive rats on the basis of structural heterogeneity of the renal papilla.

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(Presented by Academician of the Academy of Medical Sciences of the USSR D. S. Sarkisov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 99, No. 3, pp. 358-360, March, 1985. Original article submitted May 18, 1984.

0007-4888/85/9903-0362$09.50

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