AN EXPERIMENTAL STUDY OF THE REVERSIBILITY OF CARDIAC HYPERTROPHY

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Original article submitted March 18, 1963

As a result of the fact that in some cases it is now possible to correct organic defects of the heart, to restore the normal arterial pressure in hypertensive patients, and so on, a problem of much current importance is the subsequent fate of changes in the heart acquired in the course of a disease after the factors causing them have been removed.

The reversibility of myocardial hypertrophy has not been investigated systematically until very recently. The few clinical observations [1, 3, 7, 9, 13] which have been reported indicate that the roentgenological dimensions of the heart may be reduced after successful treatment of diseases associated with hypertrophy of the myocardium. However, roentgenological methods are not sufficiently precise to allow differentiation between a reduction in the dimensions of the heart as a result of disappearance of its hypertrophy and a contraction of the volume of the chambers as a result of an increase in myocardial tone and disappearance of dilatation. The few attempts which have been made to solve this problem experimentally [11, 12, 14, 15] likewise are incomplete, for their conclusions regarding the disappearance of hypertrophy were based entirely on comparison of the mean weight of control and experimental animals sacrificed at various intervals after the creation and subsequent removal of factors causing permanent hyperfunction of the heart, and were not supported by the results of histological investigation of the heart muscle.

An important obstacle retarding the experimental study of this problem has been the lack of sufficiently simple and reliable techniques for creating a marked degree of hypertrophy of the myocardium in a short time and allowing the cause to be removed at any stage of development of the process. In the experimental studies cited above the development of cardiac hypertrophy for the purpose of studying its reversibility was brought about by one of the following methods: prolonged administration of adrenalin, prolonged physical exertion, constriction of one of the renal arteries with subsequent removal of the corresponding kidney after stabilization of the arterial pressure at a high level, and the formation of an anastomosis between the right carotid artery and the right jugular vein, and its removal by ligation of the carotid artery after the development of cardiac hypertrophy. As a rule these methods did not provide a high enough degree of functional overloading of the myocardium, and did not result in the development of a high enough degree of hypertrophy.

Marked changes in the heart have been produced by the formation of experimental stenosis of the mouth of the aorta. The character and dynamics of these changes have been studied fully [6, 5]. A method of removing experimental aortic stenosis was suggested for the first time by F. Z. Meerson [6, 5], but proved to be technically difficult, especially if a long time had elapsed after formation of the stenosis on account of the development of adhesions.

D. S. Sarkisov and co-workers [2], who first began to make an extensive study of the problem of the reversibility of acute and chronic changes in internal organs, suggested an experimental model of graded and removable stenosis of the aortic orifice in rabbits. Despite its reliability, this model has certain disadvantages and, in particular, it cannot be used in small laboratory animals and requires repended surgical operations in the region of the heart.
We propose herewith a method of removable and graded coarctation of the aorta in albino rats which is simpler and more suitable for use in large-scale investigations. In the present paper we describe the results of a morphological study of the reversibility of the sequelae of persistent hyperfunction of the heart produced by the use of this method.

EXPERIMENTAL METHODS

Profiting by the method of constriction of vessels in small laboratory animals using a wire spiral, suggested by A. Kh. Kogan [4], and by the observations of Beznak [10] and M. G. Pshennikova [8], who obtained marked hypertrophy of the heart as a result of constriction of the abdominal aorta in albino rats, we wrapped a wire spiral made of unoxidizable metal around the aorta immediately below the diaphragm (laparotomy was performed through a midline incision, in layers, with the animal lying on its back). The internal diameter of the turns of the spiral corresponded to the external diameter of the aorta, so that the spiral did not compress the aorta (Fig. 1A). Next, under the turns of the spiral, between them and the aorta, was inserted the end of a thick Kapron thread, causing constriction of the aorta, narrowing its lumen by an amount equal to its cross-sectional area (Fig. 1B). The degree of coarctation of the aorta may be graded by varying the thickness of the thread or the diameter of the turns of the spiral. The free end of the thread was brought out through the cranial end of the operation wound. The abdomen was closed in layers without drainage. The free end of the thread was left beneath the skin, where it was fixed to the sutures inserted into the muscles. The operations were carried out under ether anesthesia and were completed by sprinkling penicillin solution into the abdominal cavity. To remove the coarctation at the end of the required interval after its creation, the end of the Kapron thread was palpated through the skin, a small incision made above it, and the thread pulled out of the abdominal cavity, releasing the space beneath the spiral. The spiral was left around the aorta.

For albino rats weighing 250-300 g a spiral with an internal diameter of its turns of 1.35 mm and a thread with a diameter of 0.6 mm were used, resulting in an average degree of narrowing of the cross section of the lumen of the aorta of 25%.

A morphological investigation was made of the heart of animals sacrificed 20 days after creation of coarctation of the aorta (20 rats), and also 4 months after removal of the coarctation which had been in existence for 30 days (10 rats). As controls, investigations were made of intact animals (50 rats) and animals sacrificed 4 months after the creation of a removable coarctation of the aorta (10 rats). In each rat the relative weight of the heart (ratio between the weight of the heart and live weight of the animal) was determined and a histotopographical investigation made of total sections of the myocardium stained with hematoxylin-eosin and by Van Gieson's method.

EXPERIMENTAL RESULTS

In the animals sacrificed 30 days after creation of a reversible coarctation of the aorta, the relative weight of the heart was increased and lay within the range 0.0037-0.0069 (mean 0.0047). In the intact rats at the same time it varied between 0.0027 and 0.0031 (mean 0.0029). Hence the creation of coarctation of the aorta led after one month to an increase in the mass of the heart, on average by 60%.

Total transverse sections of the hearts of these animals revealed a considerable enlargement of the chambers of the heart and thickening of the walls of the ventricles, especially the left. Histotopographical investigation revealed hypertrophy of the muscle fibers, most marked near the endo- and epicardium and in the papillary muscles (Fig. 2b). The volume of the nuclei of the fibers was increased, and individual nuclei contained vacuoles. In some areas of the myocardium, mainly at the sites of maximal development of hypertrophy, groups of fibers were seen to be undergoing degenerative changes, with areas of necrosis. These fibers were indistinct in outline, and here and there they were thinned and deformed. Their sarcoplasm was devoid of longitudinal and cross striation and appeared structureless, glassy, and homogeneous, and in some places it was broken up into granules and fragments of different shapes and sizes. These fibers stained a more intensive shade of orange-yellow with picric fuchsin, and when stained with hematoxylin-eosin they exhibited basophilia. Their nuclei were darker and structureless, and sometimes they were elongated and rod-shaped. Death of the muscle fibers was accompanied by proliferation of the loose connective tissue and accumulation of lymphoid cells, with the formation of recent scars. The stroma, mainly in the perivascular spaces, and also beneath the endo- and epicardium and, to a lesser degree, in the intermuscular spaces,