PATHOLOGICAL PHYSIOLOGY AND GENERAL PATHOLOGY

EXPERIMENTAL MYOCARDIAL INFARCTION IN CERTAIN PHYSIOLOGIC AND PATHOLOGIC CONDITIONS OF THE BODY

Article II

THE EFFECT OF CIRCULATORY SYSTEM HYPERTONIA ON THE DEVELOPMENT OF EXPERIMENTAL MYOCARDIAL INFARCTION*

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The heart's need of nourishment and of oxygen, particularly, greatly increases when the cardiac muscle is overstrained due to various factors such as great physical strain [4], raised blood pressure, cardiac defects, etc. Overstrain (overloading) of half or all of the heart is often found in myocardial infarction and seems to influence to some degree the development and healing of the infarction.

The functional overloading of the left cardiac ventricle found in hypertonia seems to have an especially unfavorable influence on the development of myocardial infarction. Coronary circulation disturbance is more frequently found, and infarction is more extensive with more serious after-effects in hypertonia patients [9,10, 11,18]. This is partially explained by the sharper atherosclerotic changes found in the coronary vessels and also by the formation of larger round platelets, the heightened permeability of the vascular walls, the frequent ruptures of the platelets, subintimal hematomas and the tendency of the vessels to spasm [1,6,15,16]. There are, however, other factors besides raised blood pressure which affect the heart unfavorably during myocardial infarction.

The purpose of this work was to find how much influence one factor, functional overloading of the myocardium (circulatory system hypertonia), has on the development and the healing of a myocardial infarction.

EXPERIMENTAL METHODS

The experiments were conducted on 56 Chinchilla rabbits, mostly males, weighing an average of 2,000-2,200 g.

A hemodynamic load on the left cardiac ventricle was caused by constricting 2/3 of the abdominal aorta under the diaphragm below the celiac artery origin, and above the orifices of the renal arteries; arterial pressure rose rapidly above the constriction. To disturb coronary circulation, an additional ligature was placed at the descending branch of the left coronary artery, always at the edge of the left cardiac auricle below the origin of the first large right branch, which, in rabbits, goes to the posterior portion of the septum. Ligation of the coronary artery was done either at the same time as coarctation of the aorta or 2-12 days later. In 6 rabbits, the coronary artery was ligated 2 months after coarctation of the aorta during prolonged hypertonia and hypertrophy of the heart. Most of the operations were performed while the animals were under Pentothal anesthesia.

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with no artificial respiration apparatus. To avoid pneumothorax, an incision was made in the center of the thoracic cavity, transecting the sternum.

We measured the blood pressure at various intervals and also took 3 standard and 3 precordial leads of the cardiac contractions and at a distance of 1,5 cm to the right and left. The clearest results were obtained in the precordial leads.

The animals died or were sacrificed by aeroembolism at different intervals in order to study the change in dynamics. The coronary vessels of the heart (in 50% of the cases) were fixed in formalin under pressure, drenched with a contrast medium and examined on stereoroentgenographs. The heart was fixed as a whole in 10% neutral formalin, imbedded in celloidin-paraffin and usually studied on longitudinal (frontal) sections, but also on some lateral, total histo-topographical sections.

The localization and size of the infarctions produced in the experimental animals were marked on cross-section drawings of the anterior and posterior halves of the heart and also on lateral sections, then compared with the control (Fig. 1). Twenty-two rabbits, in which only the descending branch had been ligated, were used as the control.

EXPERIMENTAL RESULTS

After coarctation of the abdominal aorta, the animals' blood pressure usually rose to 130-140 mm of mercury at once and continued to rise rapidly during the days following. On the 2nd-6th day, the pressure was 160-180 mm of mercury, and after 2-3 weeks, 180-200 mm of mercury, sometimes being as high as 220-240 mm of mercury. Long observation (up to 2 months) on some animals showed that the pressure usually remained high the whole time (160, 180, 200 mm of mercury). When the coronary artery was ligated in the hypertonic animals, the pressure fell to 140 and 120 mm of mercury, then rose again.

The electrocardiograms taken the first 2 weeks after coarctation of the aorta almost without exception showed changes in the waves QRS, but these changes were often indefinite and only occasionally related to a turning of the axis to the left (Fig. 2). The decline or inversion of the T waves in the standard and precordial leads was more regular. Analogous results were obtained by V. S. Smolensky [13] and F. Z. Meerson [8]. During artificial coarctation, the T wave changes in the electrocardiogram were evidently caused by the known relative insufficiency of the coronary circulation together with the increased load on the heart.

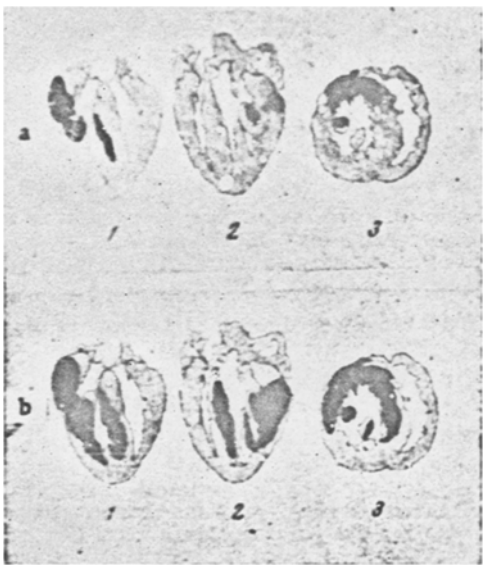

Fig. 1. Plan of localization and spread of the infarction: a) in control with 1 ligation of the anterior descending artery and b) with ligation when the left cardiac ventricle was functionally overloaded (coarctated hypertonia). 1) anterior half, seen from behind; 2) posterior half, seen from front; 3) lateral section, seen from above.

Three out of the 56 rabbits died on the operating table and 16 at various intervals after coarctation of the aorta.

The morphological changes in the myocardium during the first 2 weeks after coarctation of the aorta consisted in a protein dystrophy of the myocardial parenchyma — a thick swelling of the muscle fiber protoplasm, slight fat dystrophy, some edema of the myocardial stroma, and sometimes small extravasations. Single small foci of myomalacia, with round cell and histiocyte accumulations where the muscle fibers had died, or small proliferations of elongated cells were occasionally observed. F. Z. Meerson [8], in experiments with high (above the valves) constriction of the aorta, observed a sharper myocardial fat dystrophy as well as a considerable decrease in the glycogen concentration in the cardiac muscle during this period.

The anterior descending artery was ligated in the 38 surviving animals. Myocardial infarction was obtained in 32 animals.

Angioroentgenograms showed that the short stump of the ligated branch and the nonligated vessels were well filled with the contrast medium. The myocardial region below the ligature (the basin of the ligated vessel) was only partially filled with the contrast medium through the small anastomoses existing with the other branches of the left coronary artery and with some of the anterior branches of the right coronary artery. These anastomoses and the main trunks of the nonligated vessels were especially well expressed at later intervals after the ligation of the anterior descending artery, i.e., the 2nd and 3rd week. An especially sharp compensatory dilatation was observed in the nonligated, right posterior branch of the anterior descending artery.

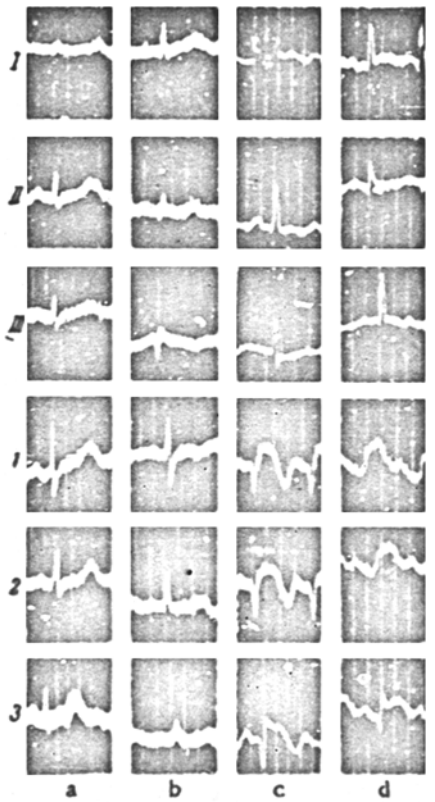

Fig. 2. Electrocardiogram taken in 3 standard and 3 precordial leads: a) original (before operation); b) after coarctation of the aorta and development of hypertonia; c) on the 3rd day after ligation of the anterior descending artery; d) on the 5th day after the development of infarction in conditions of hypertonia. I,II,III – standard leads; 1,2,3 – precordial leads.

In spite of the anastomoses, myocardial infarction regularly developed in the zone of the ligated vessel, and was usually represented by one or several, more or less large sections of myocardial necrosis and profuse cellular infiltration. The infarction was most acute 3-4 days after the coronary artery had been ligated. Subsequently, the connective tissue proliferative reaction predominated and the infarction was gradually healed by resorption of the necrosed sections and scar formation. The spread of the infarction was usually confined in the control animals to the central blood-supply zone of the ligated vessel: the part of the anterior wall of the left ventricle below the ligature, the adjoining portion of the interventricular septum and part of the anterior papillary muscle (see Fig. 1).

The extent of myocardial infarction was considerably greater in the experimental animals than in the control (see Fig. 1). Infarctions of the usual size and localization were only found in 4 of the experimental animals. In 15 rabbits, the infarction was 1½-2 times as great as that in the control, and extended over a large part of the anterior wall of the left ventricle, the anterolateral wall, the anterior papillary muscle and a considerable portion of the interventricular septum. In 10 animals, the infarction was 2-3 times greater than in the control, occupying the entire blood-supply zone of the ligated vessel, including the zone of mixed blood supply and partially invading the sections outside the blood-supply zone of the anterior descending artery: the lateral wall of the left ventricle, the posterior portion of the septum and the posterior papillary muscle (see Fig. 1). In 3 animals, it was difficult to ascertain the degree of infarction spread from morphological data, since death occurred a few hours after the ligation of the coronary artery.

In the central part of the infarction, there were usually one large or several smaller foci of myomalacia surrounded, depending on the interval since the ligation, either by a leukocyte wall, which was well expressed on the 2nd and 3rd days (Fig. 3,a), or by new granulation tissue, which gradually grew into the necrotic zone and matured until the scar stage. The whole process of necrotizing, resorbing and organizing occurred on a background of relative venous congestion, with dilated capillaries, stasis phenomena and small hemorrhages in the infarction region. The contrast medium injected into the coronary system always appeared histologically in the infarction zone, in the small and large arterial vessels, and sometimes in the capillaries. Along the periphery of the infarction, the vessels were especially dilated and filled with the contrast medium.

In a majority of cases, a direct relation was observed between the degree of aortic constriction and the size of the myocardial infarction. However, there was not always a direct relation between the degree of aortic

constriction and the blood pressure level. When the aorta was especially sharply constricted, the blood pressure did not rise, but, on the contrary, fell, and the animals often died. Evidently, the blood pressure level depended on the contractive ability of the myocardium in each specific case, as well as upon the degree of aortic constriction.

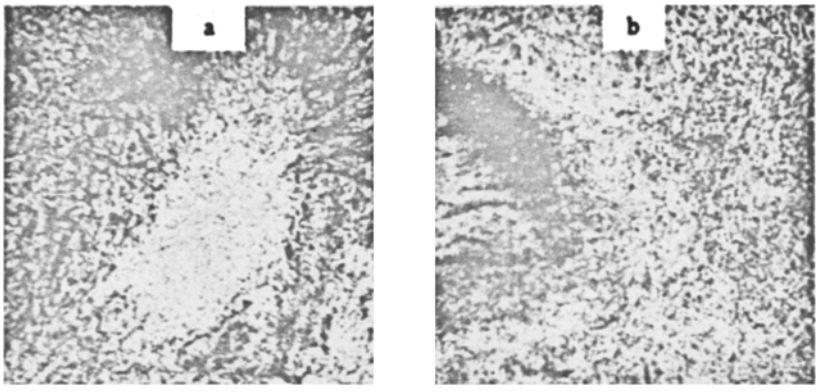

Fig. 3. Histological changes in the myocardium: a) necrosis region in the infarction zone of a control rabbit with one ligation of the coronary artery; leukocyte wall separating the necrosis zone from the surrounding live tissue; b) considerable progression of necrosis beyond the leukocyte wall which had initially separated the first development of necrosis in the myocardium. Capillaries filled with the contrast medium, small necroses and hemorrhages can be seen in the proliferation zone bordering the necrosis.

The greatest spread of the infarction occurred when the coronary artery was ligated three days after the aorta had been constricted, i.e., when the pressure above the artificial coarctation had risen to 160 mm of mercury or more. Therefore, the leading factor determining the size of the infarction, in our experiments, was the degree to which the myocardium was functionally overloaded.

In connection with the infarction spread and, possibly, with the unfavorable conditions created in the myocardium due to its functional overloading, resorption of the necrotic sections and healing of the infarction took a longer period of time than was needed in the control.

In the control animals, resorption and organization of the necrosis foci was observed on the 8th-10th day. In the experimental animals, one could still see large sections of myocardial necrosis in the central zones of the infarction on the 10th day. In some cases, the foci of necrosis remained for 25 days.

In the infarction scar, loose cellular tissue and fatty tissue grew along with the thick collagenous tissue.

The extent of the infarction and the long protraction of the healing process are shown by the changes in the electrocardiographic curve. The electrocardiogram changes were more marked in the experimental animals than in the control. The acute phase of the infarction was also prolonged, then the subacute phase occurred and further restoration of the electrocardiographic curve was retarded. In the control animals, an approximation of the segment ST to the isoline and the appearance of typical coronary waves T were usually observed as soon as the 3rd-4th day after the coronary artery had been ligated, but changes characteristic of the acute and subacute phases of the infarction were still observed on the 6th-7th day in the experimental animals (see Fig. 2).

In 5 experimental animals, a protuberance like an aneurysm formed, with a thinning of the wall on the anterior wall of the left ventricle in the upper half of the heart. According to B. B. Kogan's data [7], a cardiac aneurysm is always formed during the acute stage of the infarction, when the scar has not yet consolidated. We observed an acute aneurysm in 2 animals. In our experiments, evidently, the size of the infarctions, the

protraction of the healing period and the elevated blood pressure (exceeding 20 mm of mercury in 2 rabbits) were the cause. No aneurysms were observed to form in the normotonic control animals.

One must not overlook one more important feature. In 12 animals, signs of the progressing of the process were observed: new circulatory disturbances, hemorrhages, small foci of necrosis along the periphery of the infarction, and new round cell and histiocyte infiltrations. In 4 animals, necrosis spread beyond the limits of the original leukocyte wall (Fig. 3, b). This process progression with new zones of circulatory disturbances, ischemia and myocardial necrosis forming could be traced by the electrocardiographic changes. Newer changes were observed on electrocardiograms taken the 6th-7th day after ligation than on those taken the 3rd-4th day, when the tendency to form the coronary wave T was observed. It seemed as though the acute phase, characterized by a monophasic curve, had recurred (see Fig. 2).

Our data regarding the role of functional overloading of the heart in the development myocardial infarction agree with the data A. I. Smirnov and A. I. Shulgina [12] and with those of A. V. Smolyannikov [14]. These authors showed that circulatory disturbance of the ventricular myocardium due to ligation of the anterior descending artery was much more marked in dogs with vagal stimulation than in the control animals without vagal stimulation or intensification of the cardiac function. A. V. Smolyannikov [14] describes numerous of necrosis foci in both the zone of the ligated vessel and in other regions of the heart. The necrosis foci developed on a background of acute circulatory disturbances and resembled the picture of hemorrhagic infarction, with dilated vessels, stases and hemorrhages. Therefore, when the function is intensified, either by a hemodynamic load or by strong vagal stimulation, sharp coronary circulation disturbances occur, which expand the zone of myocardial ischemia and increase the spread of the myocardial infarction.

Obviously, besides vascular coronary circulation disturbances, the degree to which the myocardium is functionally overloaded is also an extremely important factor, as it determines the localization, spread and healing processes of the myocardial infarction. When local coronary circulation disturbances are present, functional overloading of the myocardium can produce progressive dystrophic and necrotizing processes in the myocardium.

Therefore, myocardial infarctions occurring on a background of hypertonia or attended by a temporary rise in blood pressure should be given special clinical attention.

The experimental data show that, in myocardial infarction cases, one must avoid and guard against both falling and suddenly elevated blood pressure.

There is no doubt that, when determining the condition of a patient with a myocardial infarction in order to prescribe prophylactics and treatment, the question of functional overstrain of the myocardium must be carefully considered.

SUMMARY

In order to evaluate the role of the functionally overloaded left ventricle in the development of myocardial infarction, the anterior descending artery was ligated simultaneously or after artificial hypertension was induced by coarctation of the aorta. Infarction was more prominent and healing and cicatrization were protracted for a longer time in hypertensive than in control animals. In some cases infarction even progressed, involving new portions of the myocardium. At the same time coronary wave T on the electrocardiogram disappeared while the monophasic curve appeared, thus indicating a recurrence of the acute phase.

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