PATHOLOGICAL PHYSIOLOGY AND GENERAL PATHOLOGY

EXPERIMENTAL MYOCARDIAL INFARCT IN CERTAIN PHYSIOLOGICAL AND PATHOLOGICAL STATES OF THE ORGANISM

PART 3. EFFECT OF HYPERTENSION IN THE PULMONARY CIRCULATION ON THE DEVELOPMENT OF EXPERIMENTALLY INDUCED MYOCARDIAL INFARCTION

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In our preceding two communications [4, 5] we examined the effect of graded physical exertion and of hypertension in the systemic circulation on the development of myocardial infarction. Our experiments showed that physical exertion and hemodynamic changes due to raised arterial pressure had a considerable effect on the origination and development of myocardial infarction.

The development of experimental myocardial infarction was affected to a particularly large extent by raised arterial pressure, with resulting overloading of the left ventricle, and this determined the dimensions of the lesion, its extension, and its slower healing.

In connection with these findings, we thought it would be of interest to study the effect of overloading of the right ventricle on the development of myocardial infarction, in particular on its localization and extension.

It is known that functional overloading of the right heart is encountered in a number of diseases of the lungs (emphysema, bronchial asthma, pneumosclerosis), in certain diseases of the cardiovascular system (mitral stenosis, lesions of the minor branches of the pulmonary arteries, thromboses, and pulmonary artery embolisms), and in other conditions, such as kyphoscoliosis. The heart-lung syndrome arising in these conditions represents a complex of hemodynamic disturbances with hypoxemia and functional overloading of the right heart (V. F. Zelenin [7], B. B. Kogan [8, 9], T. Durant [13], P. Soulie [15], M. Gelfand [14]). Some authors (O. Brenner [12], H. Spencer [16]) also distinguish the condition of primary hypertension in the pulmonary circulation.

These hypertensive conditions of the pulmonary circulation, hypoxia, and overloading of the right ventricle, can undoubtedly be associated with local disturbances of venous flow and with myocardial infarction. It may be supposed that the development of myocardial infarction will be particularly affected by acutely developing functional overloading of the right heart, as in bronchial asthma, pulmonary artery thromboses and embolisms, and bilateral generalized pneumonias. In such cases we encounter raised pressure in the pulmonary arterial system, together with raised venous pressure, imperfect filling of the ventricle (so-called "small heart"), lowering of the minute volume, retardation of the blood flow, increase in the volume of circulating blood, fall in systemic blood pressure, lowered basal metabolism, and hypoxemia. Within the venous system we find retardation of blood flow, together with venous stasis and obstructed lymph flow.

It is known from clinical observation that similar complexes of functional overloading of the right heart and of generalized circulatory disturbances with localized disturbances of the coronary circulation can exert a most unfavorable effect on the course and prognosis of myocardial infarction; this question has not, however, received full consideration in the published literature. It is generally believed that lesions of the right ventricle are of very rare occurrence, because of the large number of anastomoses between branches of the left and the

right coronary arteries, and of the role of the vessels of the Thebesian system, which can to some extent compensate deficient blood supply of the thin-walled right ventricle. The only literature references which we could find were to the prevalence of right sided heart lesions in emphysema (S. S. Vail [1, 2]), fat embolism of the lungs (S. A. Vinogradov [3], N. T. Raikhlin [11]), influenzal pneumonia (F. L. Leites [10]), cardio-pulmonary insufficiency (O. A. Zakharova [6]), croupous pneumonia, tuberculosis, pneumonias in children, and other conditions.

The object of the present research was to ascertain to what extent hypertension in the pulmonary circulation and overloading of the righ ventricle can affect the site, extension, and healing of a myocardial infarct, caused experimentally by ligating the anterior descending coronary artery.

EXPERIMENTAL METHODS

The experiments were performed on rabbits, of which we used 42 in all. The results were compared with those found for a second group of 36 animals, in wh'ch the coronary artery was ligated, but no other measures were taken.

In the basic series of experiments, functional overloading of the right ventricle was achieved by constricting the pulmonary artery (by means of a silk ligature, inserted under the artery) by about a third of its normal diameter, or by inducing fat embolism of the lungs. Localized disturbances of coronary circulation were produced, as in the control group, by ligation of the descending branch of the anterior coronary artery, at the margin of the left auricle, and below the point of emergence of the septal branch. Myocardial infarction was produced in 31 animals (ligation was ineffective in 4 rabbits, and the remaining 7 animals died after the first or second stage of the operation).

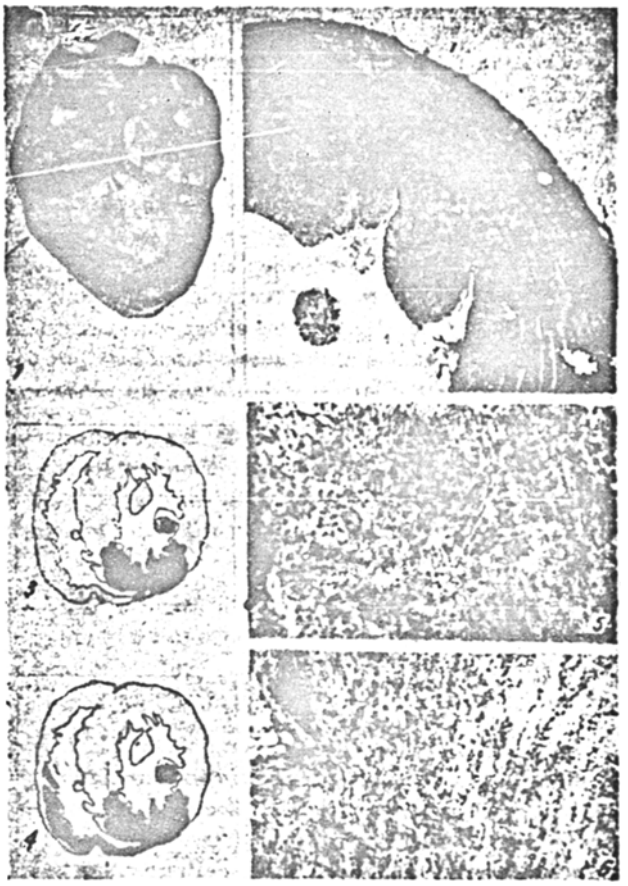
Number of Rabbits Used in Experiments on Production of Myocardial Infarction

Duration of infarction	Functional overloading of the right ventricle, caused by				
	constricting the pulmonary artery			fat embolism of the lungs	
	simultaneously	before ligation	after ligation	before ligation	after ligation
To 6 hours	—	1	—	2	—
12 »	1	—	—	1	—
24 hours	1	—	—	—	—
2 days	3	—	—	1	—
3 »	2	—	—	3	2
4 »	2	—	—	1	—
5 days	2	—	1	—	—
6 »	1	1	—	—	—
8 »	1	—	—	—	—
10 »	2	—	—	—	—
20 »	1	—	—	—	—

As a control, ligatures were placed around the pulmonary arteries of 2 animals with myocardial infarction, but were not tightened. The diameter of the lume" of the pulmonary artery of the remaining animals was reduced by about one-third. Fat embolism of the lungs was produced by injection of 1 ml of castor oil into an ear vein.

Electrocardiographic recordings were taken throughout the period of observation. Apart from the standard leads, we applied 3-5 thoracic leads (1-2 leads to the right and the left of the apex beat). After the death of the animals we filled the coronary vessels with contrast medium, and studied them by means of stereoangioroentgenograms [5]. The heart was examined in histotopographic sections, cut from the whole organ embedded in

celloidin-paraffin blocks, and stained with hematoxylin-eosin, picrofuchsin, fuchsellin, or toluidine blue, or silver-impregnated according to Gomori.



Changes in the myocardium of rabbits subjected to experimental infarction.

1) Experimental aneurysm of the right ventricle; 2) propagation of the infarct to the anterior and lateral wall of the right ventricle (duration of observation 10 days; photographed through a lens); 3) diagram showing location of an infarct caused by ligating the descending branch of the anterior coronary artery (control experiment); 4) diagram showing location and extension of an infarct under conditions of functional overloading of the right ventricle; 5) part of an infarct of the anterior wall of the left ventricle, on the 4th day after ligation of the descending branch of the anterior coronary artery; a proliferative-cellular reaction in necrotic foci, with a preponderance of histiocytes and round cells (stained hematoxylin-eosin, magnification obj. 10x, oc. 10x); 6) lateral wall of the right ventricle (from the same preparation); fresh necrosis and leucocytary infiltration-progression of the infarct, with extension to the wall of the right ventricle (fat embolism of branches of the pulmonary artery, 24 hours before killing the animal).

EXPERIMENTAL RESULTS

The stereoroentgenograms of the heart vessels of control animals showed that, as in the human, a considerable part of the anterior wall of the right ventricle is supplied by branches of the anterior descending coronary artery. Notwithstanding this, we found, in a control series of experiments, that ligation of the anterior descending branch of the left coronary artery, with resulting infarction of the anterior wall of the left ventricle and of the anterior part of the interventricular septum, did not involve the right ventricle, apart from insignificant infiltrations affecting parts immediately adjacent to the septum (see Figure, 3). Necroses of the anterior wall of the right ventricle were observed in the control group only when it had been injured by the needle, or at the level of the ligature.

Under the conditions of the experiment itself, i. e., when localized disturbances of the myocardial circulation were combined with functional overloading of the right ventricle, we found that infarction regularly extended to the anterior wall of the right ventricle (see Figure, 4). This effect was found in 24 of 29 animals, in 8 of which the lesion extended not only to the anterior, but also to the antero-lateral wall of the right ventricle. In a number of cases we also observed infarction of parts of the lateral wall of the right ventricle (8 animals; see Figure, 2).

A detailed analysis of our experimental material showed that the dimensions of the infarct and of its central necrosis in the left side of the heart, in animals with pulmonary hypertension, did not differ significantly from what was found in the control group of animals, subjected to coronary ligation alone, other than in extension of the infarct to the walls of the right ventricle. Only in 5 of this series of animals did the dimensions of the infarct and of its central necrotic focus exceed those found in the control series.

The degree of leucocyte infiltration, the preponderance of juvenile cells, and the speed of healing depended on the size of the necrotic focus. This persisted for about 10 days, and could not be seen in specimens taken 20 days after ligation. In 4 animals the process had extended chiefly towards the wall of the right ventricle, with formation of fresh foci of more recent circulatory disturbances, of necroses, and of infiltration.

In 2 or 3 animals, in which pulmonary circulation had been impeded, and right heart overloading achieved some days after ligation of the anterior descending coronary artery with formation of a left ventricular infarct, the lesions observed in the walls of the right ventricle were of more recent origin than were those of the left ventricle and the septum. Thus when a pulmonary embolism had been produced 2 days after origination of an infarct in the wall of the left ventricle, we found a proliferative-cellular reaction at the site of the infarct, with large numbers of histiocytes and round cells (see Figure, 5), whereas the wall of the right ventricle contained more recent necroses, with massive leucocyte infiltration (see Figure, 6); the animal was killed 24 hours after injection of oil.

The above observations are evidence that under conditions of raised pressure in the pulmonary circulation, with functional overloading of the right ventricle, progression of infarction can take place, with formation of fresh foci of necrosis and infiltration in the myocardium, and with extension of the infarct to the walls of the right ventricle. The extent of the right ventricular lesions was in some cases so great as to lead to attenuation of the walls, with formation of aneurysm-like bulges (see Figure, 1).

Examination of the histotopographic sections revealed foci of necrosis and cellular infiltration, among which were vessels containing contrast medium; this is evidence that these vessels were not completely shut off from the circulation. At later stages, a pronounced sclerotic process was evident in the regions affected by necrosis and infiltration, the scar tissue extending in places across the whole thickness of the wall of the right ventricle; in some places not even the subendocardial layer survived, although it usually remains intact in myocardial infarction, irrespective of its localization.

In control experiments, in which we constricted the pulmonary artery without ligating the coronary artery, we observed dystrophic changes in the wall of the right ventricle, a mucoid edema of the stroma, minute areas of proliferation and of necrosis, and subsequent mild sclerotic changes in the wall of the right ventricle.

The electrocardiographic data obtained from animals suffering from myocardial infarction complicated by functional overloading of the right heart also testify to the extent of the lesions of the anterior walls of the heart, and in general give a picture corresponding with infarctions of the extent decribed above. A more detailed analysis of these data requires a special description*.

* The electrocardiographic studies were conducted jointly with E. A. Kyandzhuntseva in the Electrocardiographic Laboratory of V. N. Vinogradov, Member AMN SSSR.

Our experimental findings on the role of functional overloading of the right ventricle in the development of myocardial infarction afford, to a certain extent, an explanation of the gravity of myocardial infarction under conditions of raised pressure in the pulmonary system, such as is present in bronchial asthma, lung embolism, and other conditions.

SUMMARY

When the anterior descending coronary artery is ligated and there is a simultaneous narrowing of the pulmonary artery or the rat emboli of the lungs the infarction usually spreads to the anterior or, in certain cases, to the antero-lateral and the lateral wall of the right ventricle in rabbits. In certain cases there were noted, likewise, the formation of the aneurysm of the right ventricle with advance of the process and appearance of fresh foci of necrosis and infiltration in the wall of the right ventricle. Thus, in the functional overstraining of the myocardium there is incoordination between the circulation of the blood and increased requirement of nutrition of the heart muscle. This brings about advancement of the process of myocardial infarction with affection of the functionally overloaded areas of the myocardium.

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