

MORPHOLOGICAL CHANGES IN THE MYOCARDIUM AFTER ALLERGIC INJURY

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The changes observed in various parts of the myocardium of 57 rabbits during experimental sensitization of the animals were investigated. The rabbits were immunized with eight daily injections of 5% antigen from whole rat heart, together with adjuvant (10-15% aluminum hydroxide gel). Histological and histochemical analysis of the myocardium of these animals showed that during sensitization destructive changes develop in its muscle fibers in association with infiltration of the stroma by lymphocytes and plasma cells. Degenerative changes develop in the muscle fibers as the result of progressive disturbances of the microcirculation due to the allergic reaction.

The harmful action of the antigen-antibody complex on the body cells and tissues has been described [3, 5, 9, 11]. The antigen-antibody reaction develops at different structural levels: cell, tissue, organ, and the organism as a whole. Changed tissue proteins possess autoantigenic properties; the change in them may be due to various factors: infection, poisoning, exposure to chemical or physical factors, etc. [1, 3, 4, 7, 11, 12]. A few reports have been published of structural and functional changes in the heart muscle in infectious-allergic myocarditis [6, 8].

This problem deserves special attention because recently an important role has been ascribed to autoimmune processes in the genesis of certain types of heart disease [10].

EXPERIMENTAL METHOD

Morphological changes were studied in the muscle of the right and left ventricles, the ventricular septum, and the atrium from 57 rabbits of both sexes and of different breeds, weighing 2.5-3.5 kg, in which an experimental autoimmune process had been produced in the myocardium [2].

The rabbits were immunized repeatedly with a 5% homogenate of whole rat heart. The homogenate was injected together with adjuvant (10-15% aluminum hydroxide gel) in the ratio of 1:1. This mixture was injected once a week in a dose of 4 ml for 8 weeks into the inguinal region on both sides alternately.

The state of autosensitization was assessed by several tests: the titer of cardiac autoantibodies, the lymphocyte and monocyte counts in the peripheral blood, the state of the coagulation system, and the succinate dehydrogenase (SDH) activity and acid phosphatase (AP) content in the peripheral blood lymphocytes.

The animals were killed by air embolism at various times during immunization (after two to eight injections of the antigen). The heart was fixed in Lillie's solution. The hearts from 18 intact animals, receiving no form of treatment, acted as the control. Pieces of tissue were embedded in paraffin wax and sections were stained with hematoxylin-eosin, picrofuchsin-fuchselin, toluidine blue, and by Heidenhain's modification of Mallory's method. The staining methods of Brachet, Feulgen, Selye, Shabadash, and Foot were used. Activity of alkaline and acid phosphatases was determined.

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EXPERIMENTAL RESULTS

After six injections of the antigen an increase in the titer of cardiac autoantibodies (up to 1:64) was found in the animals by means of the passive hemagglutination test. In the complement fixation test positive results were observed after five immunizations but the titer did not exceed 1:10. A shift of the leukocyte formula was observed in the peripheral blood, with an increase in the number of lymphocytes (60-90 per 100 leukocytes) and there was an increase in the proportion of young monocytes. This indicated irritation of the reticulo-endothelial system. Disturbances of metabolism were observed: the SDH activity was reduced and the AP concentration increased in the peripheral blood lymphocytes. Changes in the coagulation system were fluctuating in character. They were connected with the immunological changes and with the effect of the antigen on the function of the hepatocytes and, in particular, the heparinocytes. The frequency of the electrocardiographic changes increased proportionally to the number of immunizations, and the changes themselves were nonspecific. It is important to note that the changes described above appeared comparatively early, and they could therefore be used for the diagnosis of allergic damage to the myocardium.

The morphological changes differed in different parts of the myocardium and they depended on the stage of immunization.

In the early periods of immunization (2, 3, and 4 injections of the antigen) morphological signs of adaptation were found in the heart muscle (right and left ventricles, ventricular septum), where they were manifested as changes in the micro-circulation: dilatation and congestion of the capillary loops in the intermuscular stroma, amounting in some cases to stasis and petechial hemorrhages, with the appearance of a protein-containing effusion containing a few red cells in the pericapillary stroma. In the lumen of some capillaries there were PAS-positive masses staining for fibrin. The basement membranes of the stromal capillaries were friable and thickened in some places (Fig 1).

Together with vacuolation of the endothelium, it showed moderate focal proliferation with increased pyroninophilia in the cytoplasm. The interstitial stroma was friable, edematous, and rich in acid mucopolysaccharides.

Fig. 1. Congestion of arterioles. Intensive saturation of their basement membranes with PAS-positive material. Schiff's reagent, 120×.

Fig. 2. Myolysis of a muscle fiber. Focal infiltration of the stroma with lymphocytes and histiocytes. Hematoxylin-eosin, 250×.

Fig. 3. Fuchsinophilic degeneration of muscle fibers. Focal infiltration of stroma with lymphocytes and histiocytes. Selye's stain, 120×.

Foci of infiltration by lympho-histio-reticulocytes were visible in the perivascular regions. Many of the muscle fibers were in a state of granular degeneration.

Later in the course of the experiment (five and six injections of antigen) the proliferation of the endothelial cells was intensified and their cytoplasm was more strongly pyroninophilic. Phosphatase activity was reduced in the friable cytoplasm of many of the muscle fibers, and various phases of myolysis were apparent: fibrillary dissociation, fuchsinophilic degeneration, central coagulation, etc. (Figs. 2 and 3). The stroma showed increased infiltration by plasma cells. Brachet's reaction was strongly positive in the reticulocytes and plasma cells. At this stage of the experiment evidence of plasmorrhagia was particularly marked. It took the form of a strongly positive PAS-reaction of the thickened membranes of the stromal capillaries.

In the late stages of the experiment (seven and eight injections) multiple foci of atrophy of the muscle fibers and degeneration were detected. Evidence of balloon, granular, and fuchsinophilic degeneration of

the fibers was observed with a decrease in their enzyme activity and weakening of their pyroninophilia. The area occupied by muscle fibers was relatively reduced, with a corresponding increase in the area of stroma. Focal replacement sclerosis and sclerosis due to collapse were visible in the zones of degeneration and death of the muscle fibers. With the development of sclerotic changes in the myocardium, evidence appeared of a reduction in the circulation.

Analysis of the changes found in the rabbit myocardium during repeated injection of the antigen shows that the injection of a specific antigen for heart tissue is accompanied by the development of a distinctive degenerative process in the myocardium, characterized by thickening of the capillary membranes, a manifestation of autosensitization.

Degenerative changes arise in the muscle fibers, while the intermuscular stroma develops a proliferative-exudative reaction characteristic of an allergic lesion.

If the state of autosensitization is prolonged, the changes in the myocardium go on to widespread intermuscular sclerosis.

The degenerative and sclerotic changes varied in severity in different parts of the myocardium. The severest changes were observed in the left ventricle and ventricular septum, while less severe changes were found in the atria and right ventricle.

Analysis of the results showed that during sensitization widespread disturbances of the microcirculation, accompanied by marked degeneration of the muscle fibers and an autoimmune, sclerotic reaction in the stroma, develop in the myocardium of rabbits.

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